UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

May 22, 2017

PC Code: 128847
DP Barcode: 435064

MEMORANDUM

SUBJECT: **Difenoconazole**: Ecological Risk Assessment for Proposed New Uses on Guava, Papaya, Cranberry, and Watercress

FROM: Michael Lowit, Ph.D., Ecologist
Faruque Khan, Ph.D., Senior Fate Scientist
Environmental Risk Branch I
Environmental Fate and Effects Division (7507P)

Michael Lowit
Faruque A. Khan

Sankula, Sujatha
Digitally signed by Sankula, Sujatha
Date: 2017.05.22 12:46:36 -04'00'

THRU: Sujatha Sankula, Ph.D., Branch Chief
Gregory Orrick, Risk Assessment Process Leader
Environmental Risk Branch I
Environmental Fate and Effects Division (7507P)

Gregory Orrick 2017.05.22 12:39:20 -04'00'

TO: Lindsay Roe, Risk Manager Reviewer
Tony Kish, Product Manager Team 22
Cynthia Giles-Parker, Branch Chief
Fungicide Branch
Registration Division (7505P)

Sidney Jackson, Risk Manager
Marion Johnson, Branch Chief
Minor Use and Emergency Response Branch
Registration Division (7505P)

This memorandum summarizes the ecological risks associated with proposed new uses (guava, papaya, cranberry, and watercress) of the fungicide difenoconazole. Application rates, reapplication intervals, and application methods are similar to previously assessed uses. The proposed maximum single application rates range from 0.114 to 0.115 lb ai/A (ground or aerial spray and chemigation). The maximum annual application rates range from 0.34 (cranberry) to 0.46 (other proposed uses) lb ai/A.

The registrant also proposed several crop group conversions without changes in application rates or methods. *Brassica* (cole) leafy vegetable subgroup is converted to *Brassica* head and stem vegetable subgroup 5-16 and *Brassica* leafy greens subgroup 4-16b. Use on grapes is expanded to include crop group fruit, small, vine climbing, except fuzzy kiwifruit – subgroup

13-07F. These proposed changes were not considered further because previous assessments were conducted on representative crops, with the exception of watercress in subgroup 4-16b.

The current assessment relies on the findings from past risk assessments to the extent that the proposed application rates are similar, toxicity and fate data are unchanged, and models and guidance are unchanged. In that regard, the major change reflected in this assessment is the availability of new toxicity data. Three toxicity studies have been reviewed since the last risk assessment. The studies are on toxicity to a non-vascular aquatic plant (cyanobacteria; MRID 49858601) and to ten species of terrestrial plants (seedling emergence; MRID 49858602 and vegetative vigor; MRID 49858603). In addition, the current assessment also differs from past risk assessments because aquatic exposure estimates for cranberry and watercress use are based on a different set of assumptions than dry-field crops given that both crops are grown on fields that are flooded with water either intermittently (cranberry) or continuously (watercress).

1. Executive Summary

The Environmental Fate and Effects Division (EFED) evaluated the proposed new uses of the systemic broad-spectrum fungicide difenoconazole. Difenoconazole is a triazole fungicide in the conazole chemical class.[1] Fungicidal activity is attributed to the inhibition of sterol biosynthesis.[2] Sterols are important for fungi membrane structure and function. Difenoconazole is a relatively persistent compound and has three major degradates (CGA-205375, 1,2,4-triazole, and triazole acetic acid (TAA)), which are individually considered residues of concern for risk assessment purposes depending on the taxonomic group.

Consistent with previously assessed uses, the primary risk concerns from the proposed uses are for chronically exposed listed and non-listed aquatic invertebrate, fish, bird, and mammal species (**Table 1**). In addition, there is an acute risk concern for listed aquatic invertebrate species and a risk concern cannot be precluded for terrestrial dicots (listed species) or honeybees based on the available data. Although the proposed flooded-field uses (cranberry and watercress) do not trigger a level of concern (LOC) exceedance in some cases (i.e., specific taxonomic group, listed/non-listed status, and exposure scenarios as identified in **Table 1)**, there is some degree of uncertainty. This is because, as discussed in detail later, aquatic exposure may be greater than assessed depending on the water usage practices at a given cranberry or watercress production facility.

Table 1. Potential Risk Concerns Associated with the Proposed New Uses of Difenoconazole

Taxa	Direct Effects
Terrestrial and semi-aquatic plants – monocots and dicots	Yes (listed dicots)
Birds	No – Acute* Yes – Chronic[1]

[1] http://www.alanwood.net/pesticides/class_fungicides.html
[2] http://www.frac.info/home

Taxa	Direct Effects
Reptiles and terrestrial-phase amphibians[2]	No – Acute* Yes – Chronic[1]
Mammals	No – Acute* Yes – Chronic[1]
Aquatic plants	No*
Freshwater fish	No – Acute* Yes – Chronic[1]
Aquatic-phase amphibians[3]	No – Acute* Yes – Chronic[1]
Freshwater invertebrates	Yes – Acute (listed) – watercress only* Yes – Chronic[1] – cranberry (dry/flooded-field) and watercress
Estuarine/marine fish	No – Acute* Yes – Chronic[1]
Estuarine/marine invertebrates	Yes – Acute (listed) - cranberry (dry/flooded-field) and watercress* Yes – Chronic[1] - cranberry (dry/flooded-field) and watercress
Terrestrial invertebrates	No – Acute contact Uncertain – Dietary (acute and chronic)[4]

* Uncertainty regarding risk for flooded-field cranberry and watercress uses primarily depending on water use practices at the production facility (*i.e.,* exposure and risk may be greater than modeled if water is recycled). For birds and mammals, risk is for those species that prey upon fish and aquatic invertebrates contaminated with difenoconazole residues.
[1] Chronic concerns are for listed and non-listed species.
[2] Birds are surrogates for terrestrial-phase amphibians and reptiles.
[3] Freshwater fish are surrogates for aquatic-phase amphibians.
[4] Among the proposed uses, cranberry, guava, and watercress grown for seed are the most likely to provide dietary exposure to bees. Flowering, non-target plants that are attractive to bees may also provide dietary exposure. Watercress, when not grown for seed, is harvested prior to bloom and is therefore unlikely to provide dietary exposure. Papaya attractiveness to bees is unknown but plants in commercial orchards are predominantly self-pollinated hermaphrodites, reducing the likelihood of dietary exposure. Female plants require wind or insect pollination but are less common in commercial orchards.

Exposure and risk from flooded-field cranberry and watercress uses are highly dependent on the processing of water used for production. The modeled EECs are intended to represent exposure in the cranberry bog or watercress bed. They are also used to assess risk in downstream receiving water bodies (*i.e.*, waterbodies that receive the difenoconazole-contaminated water released from the bog or bed). In some cases, receiving water bodies may have lower concentrations of difenoconazole than the bog or bed (e.g., through dilution). On the other hand, the bog and bed EECs do not account for recycling of that same water back through the same or different difenoconazole-treated bogs or watercress beds. The practice of recycling may lead to greater exposure concentrations than modeled given that difenoconazole is a relatively persistent compound. Given this, risk may be underestimated in some cases as noted in **Table 1** (*i.e.*, the risk quotient (RQ) did not exceed the LOC). In summary, an LOC exceedance based on the bog or bed water indicates a potential risk concern whereas there remains uncertainty about the potential for a risk concern in the absence of an exceedance.

There are no label restrictions regarding use of difenoconazole-treated water from cranberry or watercress production for aquaculture of fish or invertebrates. To be protective, EFED recommends label restrictions to be consistent with the identified concerns about release of the difenoconazole-contaminated water into other waterbodies.

In contrast, all but one of the proposed labels contains restrictions regarding discharge of effluent containing difenoconazole into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES). In addition, effluent containing difenoconazole cannot be discharged into sewer systems without previously notifying the local sewage treatment plant authority. Those restrictions reflect and are consistent with the identified ecological concerns about release of difenoconazole-contaminated water into other waterbodies. EFED recommends adding these label restrictions to the Inspire Super label, which does not currently include them.

2. Data Gaps

The following list of data gaps[3] is generic for all proposed and current difenoconazole uses with an outdoor exposure pathway and the identified studies are not requested to support only the proposed new uses. However, there is one exception: an aquatic field dissipation study is required for use on rice. Although a study was submitted it was classified as invalid.

EFED recommends the following studies to reduce uncertainty in the risk assessment:

- Non-guideline: Chronic toxicity to benthic invertebrates (whole sediment; 3 test species: freshwater amphipod, freshwater midge, and estuarine/marine amphipod) – (difenoconazole; TGAI)[4]
    - EFED recommends that the registrant consider Agency-wide guidelines for chronic testing of freshwater and estuarine/marine organisms[5,6] because the OCSPP 850 series guidelines are in the process of being finalized. A protocol must be submitted for review prior to initiating the studies.
- Non-guideline Tier I: Honeybee adult acute oral exposure (difenoconazole; TGAI)
- Non-guideline Tier I: Honeybee adult chronic oral exposure (difenoconazole; TGAI)
- Non-guideline Tier I: Honeybee larval acute and chronic oral exposure (difenoconazole; TGAI)
- Non-guideline Tier II: Residue in pollen and nectar (recommendation pending risks identified in Tier I studies) (TEP)

---

[3] As identified in the most recent risk assessment (USEPA, 2014) and registration review problem formulation (USEPA, 2015).
[4] These studies were recently required as a condition of registration for a PRIA label amendment for EPA Reg. No. 100-739 to add new uses to the label for use on Legumes Subgroup 6C and Bushberry Subgroup 13-07B; Related to Petition #4F8231 (May 6, 2015).
[5] USEPA 2000. Methods for Measuring the Toxicity and Bioaccumulation of Sediment-associated Contaminants with Freshwater Invertebrates. EPA 600/R-99/064
[6] USEPA 2001. Methods for Assessing the Chronic Toxicity of Marine and Estuarine Sediment-associated Contaminants with the Amphipod *Leptocheirus plumulosus*. EPA 600/R-01/020

- Non-guideline Tier II: Semi-field testing for pollinators (tunnel and feeding studies) (recommendation pending risks identified in Tier I studies) (TEP)
- 850.3040: Tier III full-field testing for pollinators (recommendation pending risk identified in Tier II studies) (TEP)

In addition, submission of chronic toxicity data for major degradates of difenoconazole (1,2,4-triazole, TAA, and CGA-205375) may be useful for refining the risk concerns for birds, fish, and aquatic invertebrates.

3. General Uncertainties

- Because they are persistent, difenoconazole and its degradates may accumulate in soil after repeated use. This repeated or continuous exposure may result in significant risks to non-target organisms, especially birds and mammals. Furthermore, given that difenoconazole is also systemic, surface residues may underestimate exposure to terrestrial animals and underestimate risk.

- This risk assessment only considered the most sensitive of the species evaluated in the registrant-submitted studies. The position of the tested species relative to the distribution of all species' sensitivities to difenoconazole is unknown. Extrapolating the risk conclusions from the most sensitive tested species to non-tested species may either underestimate or overestimate the potential risks to those species.

- Several of the assessed products are mixed with another fungicide. This assessment only addresses risk from difenoconazole alone and the other active ingredients will be assessed separately. In addition, this assessment does not address possible interactions among the active ingredients that may impact the toxicity of difenoconazole.

4. Summary of Proposed Uses

The proposed application rates, reapplication intervals, and application methods are similar to previously assessed uses (**Table 2**). The proposed maximum single application rates range from 0.114 to 0.115 lb ai/A (ground or aerial spray and chemigation). The maximum annual application rates range from 0.34 (cranberry) to 0.46 (other proposed uses) lb ai/A.

The registrant also proposed several crop group conversions without changes in application rates or methods. *Brassica* (cole) leafy vegetable subgroup is converted to *Brassica* head and stem vegetable subgroup 5-16 and *Brassica* leafy greens subgroup 4-16b. Use on grapes is expanded to include crop group fruit, small, vine climbing, except fuzzy kiwifruit – subgroup 13-07F.

Table 2. Proposed Uses for Difenoconazole

Proposed Use	Maximum Application Rate[1] Minimum Application Interval[2] Application Method	End Use Products	Comments
Cranberry	0.115 lb ai/A x 3 applications (7-day interval) 0.34 lb ai/A/year of difenoconazole containing products Air, ground, or chemigation A different mode of action fungicide should be alternated after two sequential applications.	Inspire, Inspire Super, Quadris Top; Quadris Top SBX	30-day pre-harvest interval
	0.114 lb ai/A x 3 applications (14-day interval) 0.34 lb ai/A/year of difenoconazole containing products Air, ground, or chemigation A different mode of action fungicide should be alternated after two sequential applications.	Inspire XT	45-day pre-harvest interval
Watercress	0.115 lb ai/A x 4 applications (7-day interval) 0.46 lb ai/A/year of difenoconazole containing products Air, ground, or chemigation A different mode of action fungicide should be alternated after two sequential applications.	Inspire, Inspire Super, Quadris Top, Quadris Top SBX	30-day pre-harvest interval
	0.114 lb ai/A x 3 applications (7-day interval) 0.34 lb ai/A/year of difenoconazole containing products Air, ground, or chemigation A different mode of action fungicide should be alternated after two sequential applications.	Inspire XT	30-day pre-harvest interval

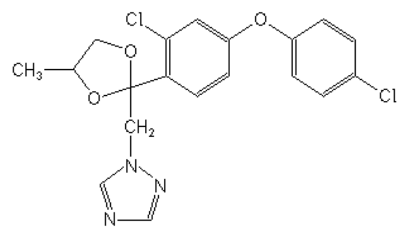
Proposed Use	Maximum Application Rate[1] Minimum Application Interval[2] Application Method	End Use Products	Comments
Guava	0.114 lb ai/A x 4 applications (7-day interval) 0.46 lb ai/A/year of difenoconazole containing products Air, ground, or chemigation A different mode of action fungicide should be alternated after two sequential applications. --- 0.115 lb ai/A x 4 applications (10-day interval) 0.46 lb ai/A/year of difenoconazole containing products Air, ground, or chemigation A different mode of action fungicide should be alternated after two sequential applications.	Inspire, Inspire Super --------------- Quadris Top, Quadris Top SBX	
Papaya	0.114 lb ai/A x 4 applications (7-day interval) 0.46 lb ai/A/year of difenoconazole containing products Air, ground, or chemigation A different mode of action fungicide should be alternated after two sequential applications. --- 0.115 lb ai/A x 4 applications (10-day interval) 0.46 lb ai/A/year of difenoconazole containing products Air, ground, or chemigation A different mode of action fungicide should be alternated after two sequential applications.	Inspire, Inspire Super --------------- Quadris Top, Quadris Top SBX	

[1] Single application rates for individual products range from 0.114 lb ai/A to 0.115 lb ai/A.
[2] All of the proposed uses require alternating to another fungicide between applications of difenoconazole-containing products. The labels do not specify an application interval between non-sequential difenoconazole applications. The minimum reapplication interval (7 days) was used for modeling purposes. In that case it was assumed that the reapplication interval is 14 days between the 2nd and 3rd difenoconazole application.

5. Fate and Transport Summary

Difenoconazole is persistent, nonvolatile, and slightly mobile in soil. The compound's log K_{ow} of 4.4 suggests a potential for bioaccumulation in the aquatic food web; however, depuration is rapid. Based on a low vapor pressure of 2.5×10^{-10} mm Hg and solubility in water of 15 mg/L, difenoconazole has a low propensity to volatilize and generate vapors after application. At test termination in laboratory studies, the organic residues that volatilized totaled 0.7% or less of the applied difenoconazole. Selected physical and chemical properties are presented in **Table 3**.

Table 3. Physical and Chemical Properties of Difenoconazole

Property	Value	Source
CAS Registry No.	119446-68-3	
Structure		MRID 46950104
Chemical Name (CAS)	1-{2-[4-(chlorophenoxy)-2-chlorophenyl-(4-methyl -1,3-dioxolan-2-yl)-methyl]} -1H-1,2,4-triazole	MRID 46950104
SMILES notation	O1CC(C)OC1(Cn2ncnc2)c3c(Cl)cc(Oc4ccc(Cl)cc4)cc3	EPI Suite, v3.12 [7]
Molecular Formula	$C_{19}H_{17}Cl_2N_3O_3$	MRID 46950104
Molecular Weight	406.27	MRID 46950104
Physical State	Red Liquid	MRID 46950104
Vapor pressure	2.5×10^{-10} mm Hg (25 ºC)	MRID 46515901
Henry's Law constant	8.9×10^{-12} atm x m^3/mol	MRID 46515901
Specific Gravity/ Density	1.14g/cm^3 @ 25 ºC	MRID 46950104
Solubility in water	15.0 mg/L @ 25 ºC	MRID 46950104
log K_{ow}	4.4 (25 ºC)	MRID 46950105

In soil, difenoconazole is persistent and slightly mobile. Difenoconazole has a low potential to reach groundwater, except in soils of high sand and low organic matter content. During a runoff event, difenoconazole will potentially enter adjacent bodies of surface water. In an aquatic environment, the main route of difenoconazole dissipation is partitioning into the bottom sediment as shown in an aerobic aquatic metabolism study (MRID 42245134), in which the distribution ratio of sediment and water phases was 8:1 at 1-day post-treatment and 40:1 at 30 days post-treatment. Difenoconazole undergoes relatively slow aqueous photolytic degradation in clear, shallow, well-lit water with a half-life of 228 days. A photolytic degradation study was also conducted with natural water resulting in a half-life of 9 days. However, it was concluded that the short half-life was primarily due to absorption by organic components present in the

[7] https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface

natural water rather than photodegradation. Overall, the data indicate that difenoconazole persists in soils and sediments in the laboratory and in the field.

The octanol water partition coefficient (log K_{ow} of 4.4) suggests that difenoconazole has a potential to bioaccumulate. Difenoconazole accumulated rapidly in edible and non-edible bluegill sunfish tissues with bioconcentration factors of 170x for edible tissues, 570x for non-edible tissues, and 330x for whole body. Depuration was also rapid with a depuration half-life of approximately 1 day and 96-98% clearance after 14 days of depuration. One metabolite, CGA-205375, was recovered from both edible and non-edible tissues, accounting for 51-64% of the applied difenoconazole. **Table 4** summarizes the environmental fate data of difenoconazole. Additional environmental fate data regarding the major degradates and maximum amounts formed can be found in the registration review problem formulation (USEPA, 2015).

Table 4. Summary of the Environmental Fate Properties of Difenoconazole

Property	Value	Source
Soil adsorption coefficient K_{oc} (L/kg)	3867, 3518, 3471, and 7734 3870, 4587, 4799, and 11202	MRID 42245135 [1] MRID 46950121
Hydrolysis half-life pH = 5 pH = 7 pH = 9	 Stable Stable Stable	 MRID 42245127
Photolysis half-life in water	ca. 9.2 days – 1mg ai/L in natural water 228 days – 1.52 ml ai/L in sterile buffer solution (15-day study)	 MRID 46950104 MRID 46950105[2]
Photolysis half-life in soil	349 - 823 days	MRID 46950106[3]
Aerobic soil metabolism half-life	84.5 days – at 0.1 ppm concentration 1600 days – at 10 ppm in loam 1059 days – at 10 ppm in sandy loam 120 days – at 0.13 ppm; Swiss loam 104 days – at 0.13 ppm; Swiss loam 165 (158) days – at 0.23 ppm; Swiss sandy loam 204 (187) days – at 0.23 ppm; Swiss sandy loam/loamy sand 204 (198) days – at 0.23 ppm; French silty clay loam 433 (408) days – at ca. 0.1 ppm in CA loamy sand at 25 ºC 533 days – at ca. 0.1 ppm in CA loamy sand at 25 ºC	MRID 42245131 MRID 42245132[4] MRID 42245133[4] MRID 46950109 MRID 46950110 MRID 46950111 MRID 46950112 MRID 46950114
Anaerobic soil metabolism half-life	947 days – at 10 ppm in loam	MRID 42245132
Aerobic aquatic metabolism half-life	860 days (10 mg ai/L) 315 (330) days (nominal 0.1 kg ai/ha =0.17 mg ai/L); Swiss pond water-silty clay loam sediment) 335 (301) days (0.17 mg ai/L; Swiss river water-sandy loam sediment) 565 days (0.04 mg ai/L)	MRID 42245134 [5] MRID 46950116 MRID 46950117
Anaerobic aquatic metabolism half-life	1245 days (10 mg ai/L) 370 days (433) (0.04 mg ai/L)	MRID 42245134 [5] MRID 46950119

Property	Value	Source
Terrestrial field dissipation half-life	252 days - determined in the 0- to 3-inch depth – CA bare loamy sand 231 days – GA bare loamy sand (four applications of 0.13 lb ai/A) 139 days – CA bare plot of loam soil (four applications of 0.13 lb ai/A) 462 days – ND bare sandy clay loam	MRID 42245140 MRID 46950126 MRID 46950127 MRID 46950129
Laboratory accumulation in bluegill sunfish bioaccumulation factor (*Lepomis macrochirus*) Depuration half-life	170x in edible tissues 570x nonedible tissues 330x for whole body 1 day	MRID 42245142

[1] There was another adsorption/desorption study (MRID 42245136) reviewed in which the test soils were autoclaved prior to conducting the study which could distort the mobility characteristic of difenoconazole, thus, the study results were not used for calculation of modeling input parameters.
[2] For modeling purposes, the longest half-life was used as it represents the most conservative scenario. However, there is considerable uncertainty in the photolysis half-lives because the duration of the studies was considerably shorter than the extrapolated half-life (MRID 46950105 and 46950106).
[3] The soil photolysis half-life under xenon light condition was recalculated to represent the conditions under natural sunlight intensity during 30-day periods between June and September (104.7-246.9 W·min/cm^2), as a result, a range of half-lives was obtained.
[4] The test application rate was significantly higher than expected under registrant-proposed use conditions for difenoconazole (MRID 42245132 and 42245133).
[5] In aquatic metabolism studies, the test application rates were significantly higher than expected under registrant-proposed use conditions for difenoconazole.

6. Exposure Summary

6.1 Residues of Concern for Risk Assessment

The residues of concern are the same as identified in the registration review problem formulation (USEPA, 2015); that is, difenoconazole and the three major degradates (CGA-205375, 1,2,4-triazole, and TAA). These degradates formed in a variety of laboratory fate studies and potentially may form in both aquatic and terrestrial environments.

Difenoconazole and CGA-205375 are considered the primary stressors of concern. Available information suggests that CGA-205375 and difenoconazole are of similar toxicity. Equal toxicity of difenoconazole and CGA-205375 is assumed in the absence of data. The other two major degradates, 1,2,4-triazole and TAA, are also considered stressors of concern; however, on a case by case basis. Available information suggests that they are equally as toxic as difenoconazole (*e.g.*, 1,2,4-triazole acute oral toxicity to rats), less toxic than difenoconazole (*e.g.*, 1,2,4-triazole and TAA acute toxicity to freshwater fish and invertebrates), or more toxic than difenoconazole (*e.g.*, 1,2,4-triazole acute oral toxicity to birds) depending on the taxonomic group and exposure scenario. For example, 1,2,4-triazole is a degradate of concern for acute toxicity to mammals and birds but is not a degradate of concern for freshwater fish and invertebrates on an acute basis or for non-vascular aquatic plants.

6.2 Terrestrial Exposure

Difenoconazole surface-residue environmental exposure concentrations (EEC) for birds and mammals were not calculated because the proposed applications rates are similar to those associated with previously assessed uses, the differences in the rates would not change past risk conclusions, new toxicity data were not received, and endpoints were not changed. Likewise, a comprehensive assessment of risk from the major degradates was conducted in two recent assessments for similar application rates (USEPA, 2014 and USEPA, 2016).

Risk was assessed for terrestrial organisms that consume aquatic organisms because aquatic exposure estimates were updated and because of the exposure potential from cranberry and watercress differs from previously assessed uses. KABAM (K_{OW} (based) Aquatic BioAccumulation Model, v 1.0)[9] was used to estimate potential bioaccumulation of difenoconazole in freshwater aquatic food webs and risk to mammals and birds that consume difenoconazole-contaminated aquatic organisms. Bioaccumulation was based on total toxic residue (TTR) EECs because the log Kow of difenoconazole (4.4) and CGA-205375 (3.79; EPISUITE estimate) suggest the potential for bioaccumulation of both compounds in the aquatic food web. Furthermore, CGA-205375 was observed in fish tissue (51%-64% of applied difenoconazole) in the available BCF study. The other two major degradates (1,2,4-triazole and TAA) have low bioaccumulation potential based on their log Kow values (-0.76 and -1.71, respectively; EPISUITE estimate) and were not considered. Representative KABAM input parameters and EECs are presented in **Appendix A**.

EECs for honeybees were not calculated because a previously assessed application rate (maximum single application = 0.13 lb ai/A; USEPA, 2014) is higher than the proposed rates and risk conclusions are not impacted by the lower rates (*i.e.*, there is not a concern for acute contact exposure). Dietary exposure was not assessed quantitatively due to a lack of toxicity data.

EECs for terrestrial plants were not calculated because the proposed rates (0.114 to 0.115 lb ai/A maximum single application) are the same as those previously assessed (0.114 to 0.13 lb ai/A maximum single application; USEPA, 2014) for aerial, ground, and chemigation applications. However, risk was assessed for the proposed use rates because new toxicity data are available since the last risk assessment.

6.3 Aquatic Exposure

TTR EECs (difenoconazole + CGA-205375) were used to characterize risk to aquatic organisms due to a lack of toxicity data. It was assumed that CGA-205375 and difenoconazole are equally toxic to all aquatic organisms based on Ecological Structure Activity Relationship (ECOSAR) estimates.[8] In a separate analysis, difenoconazole-only EECs were assessed to further characterize risk to aquatic organisms. The other two major degradates (1,2,4-triazole and TAA) were not included in TTR EECs even though there is uncertainty about their toxicity in some cases (e.g., chronic toxicity to fish and invertebrates). Certain environmental fate data for 1,2,4-triazole (average soil adsorption coefficent (K_{OC}) of 112 L/kg and solubility of 700,000 mg/L

---

[8] ECOSAR predictive software is available publically though the Epi Suite™ program. http://www2.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model

(USEPA, 2006) differ from that of difenoconazole (K_{OC} of 5381 L/kg and solubility of 15 mg/L) by one to several orders of magnitude. Consequently, using a TTR approach that combines difenoconazole, CGA-205375, 1,2,4-triazole, and TAA would not be an appropriate modeling scheme to estimate surface water EECs. In other words, there is greater certainty in the TTR estimates that exclude 1,2,4-triazole and TAA than there is in TTR estimates that include them. There is no impact on the risk conclusions in two cases: (1) when toxicity data indicate that 1,2,4-triazole and TAA are less toxic than difenoconazole and (2) when toxicity data are not available for 1,2,4-triazole and TAA and there is a potential risk concern based on TTR EECs of difenoconazole + CGA-205375. In contrast, there is some uncertainty that risk could be underestimated when toxicity data are not available and the LOC is not exceeded based on TTR EECs of difenoconazole + CGA-205375. For the proposed uses, there is little impact on the overall risk conclusions for fish and aquatic invertebrates by omitting 1,2,4-triazole and TAA because there is a risk concern based on TTR EECs of difenoconazole and CGA-205375 for some or all of the proposed uses. In some cases, there is uncertainty regarding risk from specific uses. In contrast, there is no risk concern for aquatic plants based on TTR EECs of difenoconazole + CGA-205375. However, 1,2,4-triazole is less toxic than difenoconazole to aquatic plants and TAA is likely less toxic as well given it is more structurally similar to 1,2,4-triazole than to difenoconazole.

The DT_{50}s for TTR (difenoconazole + CGA-205375) were calculated for selected environmental fate properties using the PestDF (Ver. 0.8.4; March 23, 2015) tool[9], following the NAFTA Guidance for Evaluating and Calculating Degradation Kinetics in Environmental media. Calculations of DT_{50}s in various environmental media are reported in **Appendix B**.

The EECs were generated using EFED's standard models, the Pesticide in Water Calculator (PWC) and the Pesticides in Flooded Applications Model (PFAM) for surface water[10]. The PWC is an updated version of the tool previously known as the Surface Water Concentration Calculator (SWCC). To determine EECs for cranberry use, EFED used the PWC along with the ORberriesOP scenario and, the Pesticides in Flooded Applications Model (PFAM, version 2.0). Some cranberries are grown in bogs, where the field is temporarily flooded to control pests, prevent freezing, and to facilitate harvest. The PFAM was developed specifically for regulatory applications to estimate exposure for pesticides used in flooded agriculture such as rice paddies and cranberry bogs. The PFAM model was also used in calculating aquatic exposure of difenoconazole use on watercress, an aquatic, semi-aquatic leafy vegetable. Since there is no modification of input parameters for the PWC model except for the proposed application rates of difenoconazole, a detailed description of inputs parameters can be obtained from the previous assessment (USEPA, 2014).

6.3.1 Aquatic Model Inputs for Terrestrial Uses (PWC model)

EECs were estimated using the PWC model (v1.52; December 8, 2015). The PWC is a graphical user interface that runs the Pesticide Root Zone Model (PRZM, v 5, November 15, 2006) and the Variable Volume Water Body Model (VVWM, March 6, 2014). Simulations are run for

[9] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/guidance-calculate-representative-half-life-values
[10] www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment

multiple (usually 30) years and the EECs represent peak and 21-day or 60-day mean values that are expected once every ten years based on the thirty years of daily values generated during the simulation. The PWC input parameters are shown in **Table 5.** EECs (TTR and difenoconazole-only) are presented in **Appendix C** and a representative PWC output is in **Appendix D**.

Table 5. PWC Input Parameters for TTR (Difenoconazole + CGA-205375) and Difenoconazole-Only

Parameter	Input Value and Unit	Source/Comments
Crop Guava and Papaya Cranberry (dry harvest)	**Scenario** FLavocadoSTD ORberriesOP	Surrogate scenarios were used because there are not standard scenarios available for these crops.
Maximum single application rate x maximum # of applications	Guava and Papaya 0.115 lb ai/A (0.129 kg ai/ha) x 4 Cranberry 0.115 lb ai/A (0.129 kg ai/ha) x 3	EPA Reg. No. 100-1554 EPA Reg. No. 100-1554
Method of application	Foliar Spray; CAM = 2	Product Label as above
Application efficiency	0.99 (Ground Spray) 0.95 (Aerial Spray)	Chemigation was modeled but assumed similar to ground application. EFED Model Input Guidance, Version 2.1 (USEPA, 2009a)
Spray drift	0.062 (Ground Spray) 0.125 (Aerial Spray)	USEPA, 2013a
Application date and minimum interval between applications	Guava and Papaya Relative date: Post emergence 14 days and 7-day reapplication intervals Cranberry Relative date: Post emergence 30 days and 7-day reapplication intervals	Product Labels Labels suggest application should be targeted prior or early in the disease development Assumed 14-days for application intervals between 2nd and 3rd
Hydrolysis	Stable	MRID 42245127
Aerobic soil metabolism ($t_{1/2}$) @ 25°C [a]	313 days (Parent only) *670 days (TTR)*[b]	MRID 42245131, 46950109-12, and 46950114
Aerobic aquatic metabolism ($t_{1/2}$) @ 25°C [c]	556 days (Parent only) *649 days (TTR)*[b]	MRID 46950116 and 46950117
Anaerobic aquatic metabolism ($t_{1/2}$) @ 25°C [c]	1110 days (Parent only) *1731 days (TTR)*[b]	MRID 46950119
Aquatic photolysis $t_{1/2}$ (days) [d]	Stable	MRID 46950105
Vapor pressure	2.5×10^{-10} mm Hg (25 ˚C)	MRID 46515901
Solubility in water	15 mg/L (25 ˚C)	MRID 46515901
Molecular Weight	406.27	MRID 46950104
Partition coefficient K_{oc}	5381 mL/g *3981 mL/g (TTR)*[e]	MRID 42245135 and 46950121

[a] The 90% of the UCL of the mean metabolism half-life.
[b] The 90% of the UCL of the mean metabolism half-life of TTR (*see* **Appendix B**).
[c] The 90% of the UCL of the mean metabolism half-life of all available half-lives but those obtained for high test rate. Half-life was multiplied by three (e.g., 3 x 370 days).
[d] The estimated half-life (228 days) was well beyond the duration of the study and the PWC model is not sensitive to relatively long aqueous photolysis half-lives; therefore, aquatic photolysis was considered stable for modeling purposes.
[e] Mean K_{oc} of CGA-205375

6.3.2 Aquatic Model Inputs for Flooded Uses (PFAM model)

PFAM (version 2.00; September 27, 2016) was used to estimate EECs for difenoconazole use on cranberry. The PFAM model simulates application of the pesticide to a wet or dry field and degradation in soil and/or water. If the pesticide is applied to dry soil, water may then be introduced into the field and movement of the pesticide may occur from soil into the water.

After flooding, water may be held in a holding system, recirculated to other areas of the cranberry production facility, or released to adjacent waterbodies (canals, rivers, streams, lakes, or bays) external to the cranberry fields. Potential exposure was evaluated for residues in cranberry bog water (*i.e*., flood water in the treated cranberry field). The cranberry bog water estimates are post-application residues in flood water introduced into the treated cranberry field.

The PFAM model was used to determine aquatic exposure of difenoconazole for use on watercress, which requires irrigation/flowing water during the growing period. The PFAM model was parameterized to mimic a flowing water condition in the watercress bed with a weir height of 2 inches (0.051 meters). A maximum water depth of 1.5 inches (0.0381 m) and a minimum depth of 0.5 inches (0.0127 m) were simulated based on the crop profile for watercress in Hawaii[11]. The simulation also included a no-flow period (24 hours) in the watercress bed on the application day per the proposed difenoconazole labels.

Difenoconazole concentrations in adjacent waterbodies are expected to be lower than those estimated in the watercress bed and cranberry bog water as difenoconazole can potentially degrade in the water column, be adsorbed by sediment, or diluted with uncontaminated water from other sources in the adjacent waterways. The extent of this reduction in concentrations depends on numerous factors including 1) the length of time the compound is in the water, 2) the distance the water travels, 3) the amount of dilution, and 4) whether the release water is mixed with water that also carries residues of difenoconazole. Estimates for the cranberry bog, watercress bed and release water do not account for recycling of water within the cranberry fields and watercress beds. Under some circumstances (e.g., recycled water is retreated with difenoconazole or is flooded onto a cranberry field previously treated with difenoconazole), recycling may lead to greater exposure concentrations upon release of a relatively persistent compound such as difenoconazole. Release water EECs were calculated based on 30-years of simulated results with two flooding events per year for cranberries (*i.e.*, winter flooding and flooding during harvest). The PFAM input parameters are shown in **Table 6** and details of the assumed flood schedule are presented in **Appendix E**. EECs (TTR and difenoconazole-only) are presented in **Appendix C** and representative PFAM outputs are presented in **Appendix E**.

[11] https://ipmdata.ipmcenters.org/documents/cropprofiles/HIwatercress.pdf

Table 6. PFAM Input Parameters for TTR (Difenoconazole + CGA-205375) and Difenoconazole-Only

Parameter	Input Value and Unit	Source/Comments
Crop Cranberry Watercress	**Scenario** MA_Cranberry-Winter Flood STD.PFA OR_Cranberry-Winter Flood STD.PFA WI_Cranberry-Winter Flood STD.PFA No location-specific scenario	 Interim standard scenarios *See* flood schedule assumptions in **Appendix E** *See* flood schedule assumptions in **Appendix E**
Maximum single application rate x maximum # of application	Cranberry 0.115 lb ai/A (0.129 kg ai/HA) x 3 Watercress 0.115 lb ai/A (0.129 kg ai/HA) x 4	EPA Reg. No. 100-1554
Method of application	Foliar Spray; CAM = 2	Product Label as above
Application efficiency and drift	Not applicable	PFAM Model Input Guidance, Version 2.1 (USEPA, 2016)
PFAM turn over/day	Not applicable for cranberry 7.4 (watercress)	Calculated for watercress[a]
Application date and minimum interval between applications	Cranberry Relative date: Post emergence specific date (May 15) and 7-days reapplication intervals Assumed 14-days for interval between 2nd and 3rd applications	Application date was based on the label recommendation
	Watercress Relative date: Post emergence specific date (January 15) and 7-days reapplication intervals Assumed 14-days for interval between 2nd and 3rd applications	Application date was based on the label recommendation
Hydrolysis	Stable	MRID 42245127
Aerobic soil metabolism ($t_{1/2}$)[b]	313 days (Parent only) *670 days (TTR)*[b]	MRID 42245131, 46950109-12, and 46950114
Aerobic aquatic metabolism ($t_{1/2}$)[c]	556 days (Parent only) *649 days (TTR)*[b]	MRID 46950116 and 46950117
Anaerobic aquatic metabolism ($t_{1/2}$)[d]	1110 days (Parent only) *1731 days (TTR)*[b]	MRID 46950119
Aquatic photolysis $t_{1/2}$ (days)[e]	Stable	MRID 46950105
Vapor pressure	2.5 x 10^{-10} mm Hg (25 ˚C)	MRID 46515901
Solubility in water	15 mg/L (25 ˚C)	MRID 46515901
Molecular Weight	406.27	MRID 46950104
Heat of Henry J/mol @25	54872 (25 ˚C)	Estimated (USEPA, 2016)
Partition coefficient K_{oc}	5381 mL/g *3981 mL/g (TTR)*[f]	MRID 42245135 and 46950121

[a] Flow rate of water – 10,000 gallons/day (378.5 m^3/day) [Hutchinson, 2005]
Volume of water in watercress field, assumed 1 acre field and 0.5 inches of water column in the field watercress bed 4046.8 m2*0.0127 m = 51.4 m^3
Therefore, turnover /day = 378.5/51.4 = 7.4
[b] The 90% of the UCL of the mean metabolism half-life.
[c] The 90% of the UCL of the mean metabolism half-life of TTR (*see* **Appendix B**).
[d] Half-life was multiplied by three (e.g., 3 x 370 days).
[e] Estimated half-life is beyond the duration of study, thus considered stable.
[f] Mean K_{oc} of CGA-205375

6.3.3 Monitoring Data

Monitoring data for difenoconazole were available from the United States Geological Survey (USGS) National Water-Quality Assessment (NAWQA) Program Data Warehouse[12], searched on April 21, 2017. Access to the NAWQA monitoring data is now through the Water Quality Portal (WQP) website, which integrates public available water quality data from the USGS National Water Information System (NWIS), the EPA STOrage and RETrieval (STORET) Data Warehouse, and the USDA ARS Sustaining the Earth's Watersheds Agricultural Research Database System (STEWARDS). Difenoconazole was detected in only 7 of 772 surface water samples from two states (CA and MD); the reported maximum concentration (249 ng/L) was detected in California. However, the detected concentration of monitoring data is an order magnitude lower that the EDWCs for modeled surface water. Difenoconazole was not detected at the limits of quantitation (LOQ) of 0.6 and 1.0 µg/kg-sediment and 10.5 ng/L for suspended materials in any of the 497 sediment/suspended samples collected from various states. However, the study design of NAWQA is not targeted to account for all difenoconazole use areas, timing of application, and other factors that may more accurately represent spatially and temporally dependent variables influencing runoff vulnerability. No groundwater data are available as of April 21, 2017.

Monitoring data for surface water, groundwater, and sediment from the California Department of Pesticide Regulation (CDPR)[13] were searched on April 21, 2017. No monitoring data were available for difenoconazole on CDPR's website.

7. Ecological Effects Summary

Toxicity data are summarized in **Tables 7 to 13** (*for study details see* USEPA, 2010; USEPA, 2013b; USEPA, 2014; and USEPA, 2016; *for the most recent full list of available studies see* USEPA, 2015). Previously reported ECOSAR estimates of toxicity are also summarized. Three toxicity studies submitted to support previously proposed new uses, have been reviewed since the last risk assessment. The studies are on toxicity to a non-vascular aquatic plant (cyanobacteria; MRID 49858601) and to ten species of terrestrial plants (seedling emergence; MRID 49858602 and vegetative vigor; MRID 49858603). These studies are briefly summarized below and are incorporated into this risk assessment.

The recently submitted study on terrestrial plant seedling emergence (MRID 49858602) showed no effects on monocots (NOAEC $\geq$ 0.25/0.26 lb ai/A). Corn, ryegrass, and wheat were exposed to 0.25 lb ai/A and onion was exposed to 0.26 lb ai/A. Cabbage was the only dicot affected (NOAEC = 0.13 lb ai/A, LOAEC = 0.26 lb ai/A based on reduced survival and emergence; IC_{25} was approximated as 0.25 lb ai/A). There is some degree of uncertainty in the results due to the magnitude of effects at some of the lower test concentrations. For example, for cabbage there was a 21% reduction in emergence and 16% reduction in survival at the lowest test concentration. The overall response seemed to follow a U-shaped curve. This appears to be noise in the dataset but may represent some sort of treatment-related effect. Similarly, there was

[12] http://infotrek.er.usgs.gov/nawqa_queries/jsp/swmaster.jsp
[13] http://www.cdpr.ca.gov/docs/emon/surfwtr/surfdata.htm

greater inhibition at the lowest test concentration for lettuce (23% in weight and 19% in height) and onion (19% in weight). For lettuce there was stimulation compared to the control at higher concentrations without any clear dose pattern. Onion showed an inverse response although the variability was high at all levels. Like cabbage, the overall data seem to suggest that this was noise but again it is not clear if this could have been some sort of treatment-related effect. The study is acceptable.

The recently submitted study on terrestrial plant vegetative vigor (MRID 49858603) showed effects on the growth (reduced dry weight) of one monocot (ryegrass) and one dicot species (lettuce). The NOAEC = 0.13 lb ai/A and the LOAEC = 0.26 lb ai/A for both species. The IC_{25}s are 0.368 lb ai/A and 0.299 lb ai/A for ryegrass and lettuce, respectively. No other test species showed effects. This study is acceptable.

The recently reviewed study on toxicity of difenoconazole to cyanobacteria (MRID 49858601) showed no effects up to the highest test concentration (NOAEC ≥ 4.85 mg ai/L). The study is supplemental (quantitative) due to potential solvent effects and excessive variability in the negative control. Although treatment-related effects could not be ruled out with complete certainty, the results appear more likely to primarily reflect experimental variability and there is not strong evidence to suggest that any meaningful treatment related effects occurred.

Table 7. Summary of Most Sensitive Aquatic Taxa Toxicity Endpoints for Difenoconazole

Type of Study	Species	Toxicity Value (µg ai/L)	MRID
Acute – Freshwater Fish	Rainbow trout (*Oncorhynchus mykiss*)	96-hr LC_{50} = 810	42245107
Chronic – Freshwater Fish	Fathead minnow (*Pimephales promelas*)	NOAEC = 1.9 LOAEC = 3.7 based on reduced male length of F0-generation 12 weeks post-hatch	48453205
	Rainbow trout (*Oncorhynchus mykiss*)	NOAEC = 0.86 Value used for risk assessment. Based on acute-to-chronic ratio (ACR) of fathead minnow data to rainbow trout data (the most acutely sensitive species).[1]	-
Acute – Freshwater Invertebrate	Water flea (*Daphnia magna*)	48-hr EC_{50} = 770	42245110
Chronic – Freshwater Invertebrate	Water flea (*Daphnia magna*)	NOAEC = 5.6 LOAEC = 13.0 based on reduced number of young/adult/reproductive day and adult length	42245114
Chronic – Freshwater Invertebrate (Sediment)	Midge (*Chironomus riparius*)	EC_{50} >50 mg ai/kg-sediment (nominal) NOAEC = 5 mg ai/kg-sediment (nominal) LOAEC = 50 mg ai/kg-sediment (nominal) based on emergence rate & development rate	47648601
Acute – Estuarine/Marine Fish	Sheepshead minnow (*Cyprinodon variegates*)	96-hr LC_{50} = 819	42245112

Type of Study	Species	Toxicity Value (µg ai/L)	MRID
Chronic – Estuarine/Marine Fish	Sheepshead minnow (*Cyprinodon variegates*)	NOAEC = 0.86 Based on acute-to-chronic ratio of fathead minnow data to sheepshead minnow data.[1]	-
Acute – Estuarine/Marine Mollusk	Eastern oyster (*Crassostrea virginica*)	96-hr EC_{50} = 424	42906701
Acute – Estuarine/Marine Invertebrate	Mysid shrimp (*Americamysis bahia*)	96-hr LC_{50} = 150	42245111
Chronic – Estuarine/Marine Invertebrate	Mysid shrimp (*Americamysis bahia*)	NOAEC < 0.115 LOAEC ≤ 0.115 based on reduced number of young/adult/reproductive day NOAEC = 4.8 LOAEC = 10 based on F0 post-pairing survival, offspring/female, time to first brood	46950133 49322901 and 49387801
Vascular Plant – Freshwater	Duckweed (*Lemna gibba*)	EC_{50} = 1900 EC_{05} = 110 NOAEC < 110 LOAEC ≤ 110 based on reduced frond number	46950204
Non-vascular Plant	Diatom (*Navicula pelliculosa*)	EC_{50} = 98 NOAEC = 53 LOAEC = 150 based on reduced cell density	46950208

[1] Acute toxicity to fathead minnow: LC_{50} = 1800 µg ai/L (MRID 48453201). ACR = 947

Table 8. Summary of Most Sensitive Terrestrial Taxa Toxicity Endpoints for Difenoconazole

Type of Study	Species	Toxicity Value	MRID
Acute – Avian Oral Dose	Canary (*Serinus canaria*)	LD_{50} > 2000 mg ai/kg-bw	48453202
Acute – Avian Dietary	Bobwhite quail (*Colinus virginianus*)	LC_{50} = 4579 mg ai/kg-diet	42245103
Chronic – Avian Dietary	Bobwhite quail (*Colinus virginianus*)	NOAEC = 21.9 mg ai/kg-diet LOAEC = 108 mg ai/kg-diet based on reduction in hatchling body weight	46950202
Acute – Mammalian Oral Dose	Laboratory rat (*Rattus norvegicus*)	LD_{50} = 1453 mg ai/kg-bw	42090006
Two Generation Reproduction – Mammalian	Laboratory rat (*Rattus norvegicus*)	NOAEC = 25 mg ai/kg-diet LOAEC = 250 mg ai/kg-diet	42090018
Acute Contact – Terrestrial Invertebrate	Honey bee (*Apis mellifera*)	LD_{50} >100 µg ai/bee	42245124
Acute Contact – Terrestrial Invertebrate	Earthworm	LC_{50} > 610 mg ai/kg-dw	42245125

Type of Study	Species	Toxicity Value	MRID
Seedling Emergence - Terrestrial Plants	*Inspire and Difenoconazole EC250*: Corn, Onion, Wheat, Cabbage, Lettuce, Ryegrass, Sugar beet, Soybean, and Tomato *Inspire only*: Radish *Difenoconazole EC250 only*: Oilseed rape	*Inspire* Monocot IC_{25} > 0.111/0.112 lb ai/A[1] NOAEC ≥ 0.111/0.112 lb ai/A LOAEC > 0.111/0.112 lb ai/A based on no effects (all test species) Dicot IC_{25} > 0.111/0.112 lb ai/A[1] NOAEC < 0.111/0.112 lb ai/A[2] *Difenoconazole EC250* Monocot IC_{25} > 0.25/0.26 lb ai/A[3] NOAEC ≥ 0.25/0.26 lb ai/A LOAEC > 0.25/0.26 lb ai/A based on no effects (all test species) Dicot IC_{25} = 0.25 lb ai/A* NOAEC = 0.13 lb ai/A LOAEC = 0.25 lb ai/A based on reduced cabbage survival and emergence *A sound IC_{25} could not be calculated; therefore, the IC_{25} is an approximation.	48453203 (*Inspire*) 49858602 (*Difenoconazole EC250*)
Vegetative Vigor - Terrestrial Plants		*Inspire* Monocot and Dicot IC_{25} > 0.123 lb ai/A NOAEC ≥ 0.123 lb ai/A LOAEC > 0.123 lb ai/A based on no effects (all test species) *Difenoconazole EC250* Monocot IC_{25} = 0.368 (N/A-5.17)[4] lb ai/A NOAEC = 0.13 lb ai/A LOAEC = 0.27 lb ai/A based on reduced dry weight of ryegrass Dicot IC_{25} = 0.299 (0.192-0.403)[4] lb ai/A NOAEC = 0.13 lb ai/A LOAEC = 0.26 lb ai/A based on reduced dry weight of lettuce	48453204 (*Inspire*) 49858603 (*Difenoconazole EC250*)

[1] Some species were exposed to 0.111 lb ai/A and others were exposed to 0.112 lb ai/A.
[2] Effects at 0.11 lb ai/A on lettuce, sugar beet, and soybean were considered biologically significant. Lettuce showed reduced emergence (21%), survival (17%), shoot length (26%), and dry weight (24%). Soybean showed reduced shoot length (23%). Sugar beet showed reduced survival (18%).
[3] Corn, ryegrass, and wheat were exposed to 0.25 lb ai/A and onion was exposed to 0.26 lb ai/A.
[4] Range is 95% confidence interval.

1,2,4-triazole (PC 600074)

Available guideline data are presented in **Tables 9** and **10**. 1,2,4-triazole is less toxic than difenoconazole to non-vascular plants (green algae), freshwater fish (acute basis), and freshwater invertebrates (acute basis). In contrast, birds are more acutely sensitive to 1,2,4-triazole compared to difenoconazole. Finally, both 1,2,4-triazole and difenoconazole showed chronic effects to mammals at 250 mg ai/kg-diet; however, there is uncertainty about the relative chronic toxicity of the two compounds because a NOAEC was established in the difenoconazole study (25 mg ai/kg-diet) whereas the 1,2,4-triazole study did not test below 250 mg ai/kg-diet.

Non-guideline, summary report data on acute oral toxicity to rats (MRID 45284001, 45284004, and 45284008) suggests that 1,2,4-triazole (LD_{50}s ranging from 1375 to 3080 mg/kg-bw) and difenoconazole (LD_{50} = 1453 mg ai/kg-bw) are equally as toxic.

A non-guideline study with freshwater fish (MRID 45880405) showed no effects on the growth rate of juvenile rainbow trout after 28 days of exposure to 99.2 mg ai/L. Sublethal effects were observed at concentrations of 9.87 mg ai/L and higher (resting on the bottom, labored respiration, and low activity). There is not a comparable study conducted with difenoconazole.

ECOSAR methods were used to predict 1,2,4-triazole toxicity to fish and invertebrates based on its structural similarity to chemicals for which aquatic toxicity data are known (**Appendix F**). Estimates were available for freshwater organisms but not marine/estuarine organisms. A comparison of 1,2,4-triazole ECOSAR estimates to experimentally derived difenoconazole toxicity values suggests that 1,2,4-triazole is much less toxic (two orders of magnitude) than difenoconazole on a chronic basis to freshwater invertebrates and fish. There is reasonable confidence in the ECOSAR estimates for 1,2,4-triazole (at least for fish and non-vascular plants[14]) given that the ECOSAR estimates are within an order of magnitude of the available experimentally derived values.

Table 9. Summary of Most Sensitive Aquatic Taxa Toxicity Endpoints for 1,2,4-Triazole

Type of Study	Species	Toxicity Value (µg ai/L)	MRID
Acute – Freshwater Fish	Rainbow trout (*Oncorhynchus mykiss*)	96-hr LC_{50} = 498,000	48474301
Acute – Freshwater Invertebrate	Water flea (*Daphnia magna*)	48-hr EC_{50} > 98,100	48453206
Non-vascular Plant	Green algae (*Pseudokirchneriella subcapitata*)	EC_{50} = 14000 NOAEC = 3100 LOAEC = 6800 based on reduced area under the growth curve	45880401

Table 10. Summary of Most Sensitive Terrestrial Taxa Toxicity Endpoints for 1,2,4-Triazole

Type of Study	Species	Toxicity Value	MRID
Acute – Avian Oral Dose	Bobwhite quail (*Colinus virginianus*)	LD_{50} = 770 mg ai/kg-bw	49380701

[14] There is no basis for judging confidence in the ECOSAR estimate of acute toxicity to freshwater invertebrates due to a non-definitive endpoint.

Type of Study	Species	Toxicity Value	MRID
Two Generation Reproduction – Mammalian	Laboratory rat (*Rattus norvegicus*)	NOAEC < 250 mg ai/kg-diet LOAEC ≤ 250 mg ai/kg-diet	46467304

Triazole Acetic Acid (PC 600082)

Available data are presented in **Tables 11** and **12**. TAA is less acutely toxic than difenoconazole to mammals, freshwater fish, and freshwater invertebrates. It is uncertain if TAA is more or less acutely toxic to birds than difenoconazole because none of the available studies for either chemical showed treatment-related mortality up to the highest doses tested (ca. 2000 mg ai/kg-bw).[15] No other data are available.

A comparison of TAA ECOSAR estimates to experimentally derived difenoconazole toxicity values suggests that TAA is much less toxic (three or more orders of magnitude) than difenoconazole to aquatic non-vascular plants, freshwater fish (chronic basis), and freshwater invertebrates (chronic basis) (**Appendix F**). Estimates were not available for marine/estuarine organisms. There is no basis for judging confidence in the ECOSAR estimates because the ECOSAR estimates for acute toxicity to fish and invertebrates are substantially greater (less toxic) than the non-definitive endpoints observed in the available acute toxicity studies.

Table 11. Summary of Most Sensitive Aquatic Taxa Toxicity Endpoints for Triazole Acetic Acid

Type of Study	Species	Toxicity Value (µg ai/L)	MRID
Acute – Freshwater Fish	Rainbow trout (*Oncorhynchus mykiss*)	96-hr LC_{50} > 101,000	48453209
Acute – Freshwater Invertebrate	Water flea (*Daphnia magna*)	48-hr EC_{50} > 108,000	48453208

Table 12. Summary of Most Sensitive Terrestrial Taxa Toxicity Endpoints for Triazole Acetic Acid

Type of Study	Species	Toxicity Value	MRID
Acute – Mammalian Oral Dose	Laboratory rat (*Rattus norvegicus*)	LD_{50} > 5000 mg ai/kg-bw	45596802
Acute – Avian Oral Dose	Bobwhite quail (*Colinus virginianus*)	LD_{50} > 1926 mg ai/kg-bw	49412601

CGA-205375

On an acute oral basis, CGA-205375 (LD_{50} = 1289 mg ai/kg bw) and difenoconazole (LD_{50} = 1453 mg ai/kg bw) are of similar toxicity to mammals (**Table 8 and 13**). No other data are available.

A comparison of CGA-205375 ECOSAR estimates to experimentally derived difenoconazole toxicity endpoints suggests that CGA-205375 is not more toxic than difenoconazole to aquatic

[15] There was one mortality in the canary study (MRID 48453202) that may not have been treatment related.

organisms in general and is similar in toxicity (< 10 times difference) to aquatic non-vascular plants, fish (acute basis), and invertebrates (acute basis) (**Appendix F**). The available information also suggests that CGA-205375 and difenoconazole are similar in chronic toxicity to freshwater fish and invertebrates based on ECOSAR estimates of both compounds (< 10 times difference) and to a lesser extent when based on comparison of CGA-205375 ECOSAR estimates to experimentally derived difenoconazole data. CGA-205375 data are not available to judge the level of confidence in the ECOSAR estimates.

Table 13. Summary of Most Sensitive Terrestrial Taxa Toxicity Endpoints for CGA-205375

Type of Study	Species	Toxicity Value	MRID
Acute – Mammalian Oral Dose	Mouse	LD_{50} = 2309 mg ai/kg-bw[1]	46950303

[1] LD_{50} = 1289 mg ai/kg-bw scaled to laboratory rat weight (350 g) based on an average mouse body weight of 34 g in this study and the following equation: mouse LD_{50} * (mouse bw/rat bw)$^{0.25}$

7.1 Incidents

Reviews were conducted of the PRISM Incident Data System (IDS)[16] and the Agency's Aggregated Incidents Reports database on May 18, 2017. The Avian Incident Monitoring System (AIMS)[17] was last reviewed on November 21, 2014 (the database has not been updated in the interim). No incidents were reported in AIMS.

Ten minor incidents of damage to plants (unspecified species) were reported for one difenoconazole product (Revus Top) in the aggregated incident database. Revus Top is a dual ai product containing mandipropamid, a fungicide, as well as difenoconazole. Three incidents are reported in IDS for damage to grapes, all with a certainty of "possible" for difenoconazole as a causal agent. Two of the incidents involve application of Revus Top and the other incident involves application of Inspire Super, a dual ai product containing cyprodinil, a fungicide, as well as difenoconazole. The incidents resulted in necrotic browning and death.

In addition, three other incidents associated with difenoconazole were added to the IDS database since the last risk assessment in 2016. Each incident has a certainty of "unlikely" for difenoconazole as a causal agent. Two of the incidents occurred in Canada and involved mortality of honeybees. One of those was associated with Cruiser Maxx Vibrance, a multi ai product containing three fungicides (difenoconazole, sedaxane, and metalaxyl) and an insecticide (thiamethoxam). The product associated with the other honeybee incident is unknown but insecticides were also applied in the vicinity of the incident. The third incident involved mortality of red winged blackbirds and the product Dividend Extreme, a dual ai product containing mefenoxam, a fungicide, as well as difenoconazole.

Unlike Inspire Super, no incidents were reported for the other four assessed products (Inspire, Inspire XT, Quadris Top, and Quadris Top SBX), which do not contain any of the active ingredients (other than difenoconazole) in the products associated with the reported incidents.

---

[16] Previously known as the Ecological Incident Information System (EIIS) www.epa.gov/espp/consultation/ecorisk-overview.pdf
[17] www.abcbirds.org/abcprograms/policy/toxins/aims/aims/index.cfm

8. Ecological Risk Summary

8.1 Potential Risks of Difenoconazole Exposure to Terrestrial Organisms

8.1.1 Birds and Mammals

As in past risk assessments of similar application rates there is not an acute risk concern for birds or mammals from the proposed uses. However, there is a chronic risk concern for both listed and non-listed bird and mammal species as was determined for previously assessed uses.

Surface-residue exposure

Risk from exposure to surface-residues was not reassessed because the proposed application rates are similar to previously assessed rates and the associated risk conclusions are applicable to the proposed uses.[18,19] There is not an acute concern for birds or mammals from the proposed uses. However, there is a chronic risk concern for both listed and non-listed bird and mammal species

Due to a lack of data, this risk assessment may underestimate acute risk to birds (*no data*: CGA-205375) and mammals (*no data*: 1,2,4-triazole) if the degradates are substantially more toxic than difenoconazole.[20] Furthermore, difenoconazole degradates may contribute to the chronic risk concern for birds (*no data*: 1,2,4-triazole, TAA, and CGA-205375) and mammals (*no data*: TAA and CGA-205375) to the extent that their toxicity equals or exceeds that of difenoconazole. Submission of additional toxicity data could be useful for better refining the likelihood of risk.

Contaminated aquatic organism exposure

Risk from exposure to contaminated aquatic organisms (*i.e.*, prey of birds and mammals) was assessed because water exposure estimates were updated and because of the exposure potential from cranberry and watercress use differs from previously assessed uses. Risk concerns are the same as those for previously assessed uses (e.g., USEPA, 2014 and USEPA, 2016) with one exception. Like previous findings, there is a potential chronic risk concern for mammals; however, unlike previous findings, there is not a chronic risk concern for birds because the relevant assessed exposure estimates (*i.e.*, the combination of pore and overlying water concentrations) are lower than those associated with previously assessed uses.

There is not an acute risk concern for birds or mammals from the proposed uses (RQs $\leq$ 0.01; listed species LOC = 0.10; **Table 14**). Likewise, there is not a chronic risk concern for birds

[18] USEPA, 2007; USEPA, 2009b; USEPA, 2010; USEPA, 2014; and USEPA, 2016. These previously assessed uses showed no acute risk concern for the same application rate as proposed or in the case of the proposed cranberry use, rates with a greater number of applications. In other words, the previously assessed uses have higher annual application rates and thus EECs for cranberry. Although the data were not shown, the most recent assessment (USEPA, 2016) found no acute avian risk concern from exposure to 1,2,4-triazole even assuming a single application of 0.52 lb ai/A, which is higher than the annual application rate of any of the proposed uses.

[19] The chronic LOC is exceeded for both birds and mammals even for a single annual application (1 x 0.114 lb ai/A; USEPA, 2013b) that is equal to the proposed maximum single application rate (0.114-0.115 lb ai/A).

[20] Non-guideline summary data suggests that 1,2,4-triazole and difenoconazole are equal in acute toxicity to rats.

(RQs ≤ 0.79; non-listed/listed species LOC = 1.0). In both cases, this conclusion is within the context of the limitations of the exposure modeling (*see* **Section 8.2.4** regarding uncertainty for flooded-field cranberry and watercress); therefore, the potential exposure and risk may be underestimated.

Table 14. RQs for Proposed Use of Difenoconazole for Wildlife Feeding on Aquatic Organisms[1,2,3,4]

Crop	Representative Wildlife Species of Different Feeding Groups	Acute RQ		Chronic RQ	
		Dose Based	Dietary Based	Dose Based	Dietary Based
Wisconsin wet harvest/winter flood cranberry bog water (highest TTR EECs) and Guava/papaya; ground application (lowest TTR EECs)	*Mammalian*				
	fog/water shrew	<0.01	N/A	0.63-**3**[#]	≤0.47
	rice rat/star-nosed mole	<0.01	N/A	0.77-**3**[#]	≤0.47
	small mink	<0.01	N/A	0.99-**4**[#]	≤0.66
	large mink	<0.01	N/A	**1.1-5**	≤0.66
	small river otter	<0.01	N/A	**1.2-5**	≤0.66
	large river otter	<0.01	N/A	**1.4-6**	≤0.69
	Avian				
	sandpipers	≤0.01	<0.01	N/A	≤0.54
	cranes	<0.01	<0.01	N/A	≤0.55
	rails	<0.01	<0.01	N/A	≤0.63
	herons	<0.01	<0.01	N/A	≤0.65
	small osprey	<0.01	<0.01	N/A	≤0.75
	white pelican	<0.01	<0.01	N/A	≤0.79

[#] The RQ > LOC (1.0) for all proposed use scenarios except ground application on guava/papaya.
[1] Range is based on the proposed uses resulting in the lowest and highest TTR EECs (Guava/papaya – ground application and Wisconsin cranberry (bog water: wet harvest and winter flood); **Appendix C, Table C-1**).
[2] Concentration in water is based on an averaging period of 4 days (closest TTR EEC to the 9-day KABAM estimated time to steady state). For wet harvest/winter flood cranberry and watercress the 1-day TTR EEC was assumed equivalent to the 4-day TTR EEC because the model does not provide 4-day pore water concentrations.
[3] RQs greater than 2 (chronic) are rounded to the nearest whole number.
[4] It is assumed that the toxicity of CGA-205375 is the same as difenoconazole in the absence of data. Acute RQs for mammals are based on difenoconazole toxicity (LD_{50} = 1453 mg ai/kg bw for rat); however, risk conclusions for acute risk to mammals would not change if based on CGA-205375 toxicity (LD_{50} = 2309 mg ai/kg bw for mouse).
BOLD indicates that the RQ is greater than or equal to the chronic LOC (1.0).
N/A = not applicable

There is a chronic risk concern for mammals from all proposed uses (RQs > 1 for dose-based exposure; LOC = 1.0). On the other hand, the LOC is not exceeded for dietary based chronic exposure. The potential risk concern is broad-based because it extends to mammals in three different feeding groups (consuming fish, benthic invertebrates, filter feeders, or some combination thereof) and a range of body sizes within those feeding groups. The only exception is for ground applications on guava and papaya. In that case the potential concern is primarily for mammals that consume medium to large sized fish (represented in the model by mink and river otters).

The chronic concern based on cranberry bog water and watercress beds includes piscivorus species (*i.e.*, those that consume fish) as well as those that consume benthic invertebrates and filter feeders. In some cases, mammals that consume benthic invertebrates and filter feeders would potentially be more impacted than those that consume only fish at production facilities that attempt to actively exclude fish from bog water. On the other hand, fish are also representative of aquatic-phase amphibians (e.g., salamanders and frogs) which may be more difficult to actively exclude from water used to flood the fields. Likewise, fish may or may not be present in the watercress beds depending on the practices at an individual facility and any fish in the beds would be limited in size due to the shallow depth of flooding (e.g. ≤ 2 inches). Nonetheless, fish and aquatic-phase amphibians in receiving waters may be exposed to resides in the release water from cranberry bogs and watercress beds and they may consume contaminated (*i.e.*, containing difenoconazole and CGA-205375 residues) lower trophic-level organisms residing in the water released from the difenoconazole-treated bogs and beds.

It is a reasonable expectation that mammals may be exposed to difenoconazole-contaminated prey from flooded-field cranberry and watercress use. This is because wildlife will likely be attracted to areas where aquatic agriculture occurs given the presence of resources (*i.e.*, aquatic animals) in waterbodies associated with production including source water, cranberry bogs, watercress beds, and any receiving waterbodies that receive outflow from the bogs and beds.

There is some uncertainty about the chronic risk concern for mammals because the BCF study showed a depuration half-life of one day for all radiolabeled compounds (*i.e.*, difenoconazole, CGA-205375, and any other degradates). Although the study suggests rapid loss of bioaccumulated difenoconazole and CGA-205375 from fish when exposure is removed under laboratory conditions, difenoconazole is persistent in the environment. Thus, under some circumstances there may be reduced risk for terrestrial wildlife that consume aquatic organisms; for example, sustained bioaccumulation may be lower in aquatic food webs only temporarily or sporadically exposed to difenoconazole (e.g., in sections of flowing water bodies with pulses of difenoconazole and CGA-205375). In contrast, bioaccumulation may be greater and more sustained for food webs in static water bodies because it is likely to take longer for difenoconazole to dissipate from these aquatic environments.

The assessment included CGA-205375 because it is assumed that CGA-205375 toxicity is the same as difenoconazole due to a lack of data (acute for birds and chronic for birds and mammals) and because CGA-205375 is expected to bioaccumulate like difenoconazole. In general, the conclusions are insensitive to this assumption. Risk conclusions are the same for acute toxicity to mammals based on either the available difenoconazole or CGA-205375 toxicity data (analysis not shown). The lack of an acute or chronic risk concern for birds would only change if CGA-205375 is more toxic than difenoconazole. The potential chronic risk concern for mammals is not impacted by CGA-205375 toxicity because there is a concern based on difenoconazole-only EECs (analysis not shown; *see* exception[21]); however, the level of confidence in the concern could change if CGA-205375 toxicity differs from difenoconazole.

[21] The one exception is ground application to guava and papaya. The LOC is not exceeded for any feeding groups or representative mammals when based on only difenoconazole exposure.

8.1.2 Terrestrial Plants

Although exposure from the proposed uses is the same as previously assessed uses (USEPA, 2014), risk was assessed because new toxicity data are available for a second typical end use product (TEP; Difenoconazole EC250).

There is not a risk concern for monocots (non-listed or listed species) or non-listed dicot species from the proposed uses. This conclusion is based on EECs reported in a previous risk assessment (USEPA, 2014) and available toxicity data for two TEPs (RQs < 1; LOC = 1.0 for listed and non-listed species).

Risk to listed dicot species is less clear. There is not an exceedance of the LOC based on exposure to one of the TEPs, Difenoconazole EC250.[22] On the other hand, results of seedling emergence testing with the other TEP, Inspire, showed effects to dicots at a concentration (0.111 lb ai/A) that approaches those that could be a risk concern for listed dicot species. In that study, statistical significance was not detected between the test concentration and control. However, the lack of statistical significance for three of the dicots (lettuce, soybean, and sugar beet) may have been due to the high experimental variability and the magnitude of some of the effects is considered potentially biologically significant. Lettuce showed reduced emergence (21%), survival (17%), shoot length (26%), and dry weight (24%). Soybean showed reduced shoot length (23%). Sugar beet showed reduced survival (18%). EECs are less than the non-definitive NOAEC for Inspire; however; the NOAEC would need to be only about four to five times lower than 0.111 lb ai/A to have a risk concern for semi-aquatic listed dicots. The difference would need to be greater (at least 14 times lower) to have a risk concern for plants located in dry areas or for plants only exposed to difenoconazole through spray drift. Risk to listed dicot species cannot be precluded based on the Inspire TEP given the presumed biological significance and magnitude of the observed inhibition at 0.111 lb ai/A for lettuce, soybean, and sugar beet.

Although there was not an LOC exceedance for dicots with the Difenoconazole EC250 TEP, there is some degree of uncertainty regarding potential effects from exposure to that TEP as well due to the magnitude of effects in several species (all dicots except onion) observed at some of the lower test concentrations in the seedling emergence study. The overall study data suggest that the responses represented background noise but at the same time it is possible that the responses could have been treatment-related effects representing non-typical dose responses. A potentially confounding factor when interpreting treatment-related effects from a fungicide is that the results may reflect some combination of direct effects on the plants as well as indirect effects through control of fungus that may cause either stimulation or inhibition. Indirect effects could add considerable variability, making it difficult to discern treatment-related effects in a laboratory study. Furthermore, the presence or absence of any interacting fungus could also add variability to the manifestation of any effects on plants in the environment.

Finally, there are incidents associated with difenoconazole containing products that suggest that some plants (dicots) may be sensitive to exposure. One dual ai (difenoconazole and mandipropamid) product, Revus Top, was associated with ten incidents of minor damage to plants (unspecified species) and two incidents of necrotic browning and death to grapes;

[22] Based on EECs presented in USEPA, 2104. RQs < 1 and LOC = 1.0 for listed and non-listed species.

however, it is uncertain if the product caused the damage or if so then which of the fungicides may have contributed. There is one additional incident of necrotic browning and death to grapes associated with the application of Inspire Super, another dual ai (difenoconazole and cyprodinil) fungicide product. Although some difenoconazole containing products may elicit plant sensitivity, no incidents were reported for the currently assessed products except for Inspire Super.

In summary, there is not a risk concern for monocots or non-listed dicots based on the available data. Nonetheless, it is not uncommon for fungicides to impact plants (Petit et al, 2012) and the data, analysis, and incidents suggest that the proposed use of difenoconazole could elicit effects in some sensitive dicot species. Those effects may be from TEP-specific exposure and may be dependent on plant-fungus interactions.

8.1.3 Terrestrial Invertebrates

There is not an acute contact risk concern for a single application rate of 0.13 lb ai/A (USEPA, 2014); therefore, there is not a concern for the lower single application rates (0.114 to 0.115 lb ai/A) of the proposed uses. However, there is uncertainty about risk from dietary exposure (acute and chronic) due to a lack of toxicity studies. The potential risk concern from dietary exposure is dependent not only on the application rate, timing, and method but also on the attractiveness of the plant species containing difenoconazole residues and whether or not the species is dependent upon bee pollination. There is greater potential for dietary exposure to residues on pollen and nectar of cranberry and guava plants than to those on watercress (unless grown for seed) or papaya plants (**Table 15**). Cranberry, watercress, and guava are attractive to bees; however, in some cases watercress is less likely to provide dietary exposure to bees because it is harvested prior to bloom when it is not grown for seed. Furthermore, cranberry and guava require bee pollination. EFED is unsure of the attractiveness of papaya to bees; however, papaya plants in most commercial orchards would not require bee pollination because they are typically hermaphrodites, which can self-pollinate. In contrast, female papaya plants do not self-pollinate and it has been suggested that wind and insects (e.g. thrips and moths) may contribute to pollination. Like the proposed crops, the same factors impacting dietary risk apply to any non-target plants that inadvertently receive difenoconazole residues.

Risk to earthworms appears to be low for the proposed uses based on the conclusions for a higher application rate (0.56 lb ai/A/season[23]; USEPA, 2007).

[23] Risk was assessed based on the seasonal rate only. Although the modeled rate was 0.56 lb ai/A/season, it appears that this was in error. Previous, current, and proposed labels (Inspire and Alibi Flora) state a seasonal, crop, or annual maximum of 0.52 lb ai/A for ornamental use.

Table 15. Crop Attractiveness to Bees and Crop Reliance on Bees for Pollination

Crop	Attractiveness[1]				Requires Bee Pollination?	Uses Managed Pollinators?	Comments *Source*
	Honeybee (Pollen)	Honeybee (Nectar)	Bumble Bees (Flower)	Solitary Bees (Flower)			
Cranberry	+	+	++	++	Yes	Yes	*USDA (2014)*
Watercress	++	++	+	+	No	No	Extrapolated from mustard seed and cabbage. Harvested prior to bloom when not grown for seed production. *USDA (2014)*
Guava	Honeybee is the main pollinator.		?	?	Yes	?	*https://www.crfg.org/pubs/ff/guava.html*
Papaya	?	?	?	?	No	?	Wind may be main source of pollination but insects may contribute. Commercial orchards may rely on hermaphrodites which can self-pollinate. *https://www.crfg.org/pubs/ff/papaya.html* *https://www.wifss.ucdavis.edu/wp-content/uploads/2016/10/Papayas_PDF.pdf*

[1] Attractiveness is a qualitative metric based on the inherent attractiveness of a crop (*i.e.*, the pollen and nectar) (USDA, 2014)
+ Attractive under certain conditions
++ High attractiveness

8.2 Potential Risks of Difenoconazole Exposure to Aquatic Organisms

8.2.1 Fish

There is not an acute risk concern for fish from the proposed uses within the context of the limitations of the exposure modeling (*see* **Section 8.2.4** regarding uncertainty for flooded-field cranberry and watercress). The acute listed-species LOC (0.05) is not exceeded for freshwater or estuarine/marine fish (RQs ≤ 0.048; **Table 16**).

Table 16. Acute Risk Quotients for Freshwater and Estuarine/Marine Fish Exposed from the Proposed Difenoconazole Uses (TTR EEC)

Use	Peak EEC (µg/L)[1]	Freshwater Acute RQ (LC_{50} = 810 µg/L)	Estuarine/Marine Acute RQ (LC_{50} = 819 µg/L)
Guava/Papaya	3.2-5[2]	<0.01	<0.01
Cranberry (dry harvest)	5.7-8.3[2]	≤0.01	≤0.01
Cranberry (wet harvest & winter flood – bog water)	10.5-11.8[3]	≤0.015	≤0.014
Watercress	38.70	0.048	0.047

[1] *See* **Appendix C, Table C-1**.
[2] Range representing ground and aerial applications.
[3] Range representing scenarios resulting in the lowest (Oregon) and highest (Wisconsin) 1-day average TTR EECs for aerial applications.
BOLD exceeds acute listed-species LOC (0.05).

There is a chronic risk concern for fish (listed and non-listed species) from all of the proposed uses. The chronic LOC (1.0) is exceeded for freshwater and estuarine/marine fish (RQs > 1) based on TTR EECs (**Table 17**). Despite uncertainty about degradate chronic toxicity[24], it is important to note that the chronic LOC is exceeded based on difenoconazole-only EECs as well for all use scenarios (60-day EECs > 0.86 µg/L in **Table C-1**, **Appendix C**). The potential risk concern is for fish in the cranberry bog, watercress bed, and receiving water bodies. In some cases, cranberry bog water may not contain fish if attempts are made to actively exclude them from source water. On the other hand, even if fish are actively excluded from flood waters, they are also representative of aquatic-phase amphibians (e.g., salamanders and frogs) which may be more difficult to actively exclude from the bog. Likewise, fish may or may not be present in the watercress beds depending on the practices at an individual facility and any fish in the beds would be limited in size due to the shallow depth of flooding (e.g. ≤ 2 inches). Nonetheless, fish and aquatic-phase amphibians in receiving waters may be exposed to resides in the release water from cranberry bogs and watercress beds.

Although there is an exceedance of the chronic LOC for both freshwater and estuarine/marine fish residing in bog water or watercress beds; it is assumed that freshwater is used for flooding cranberry bogs and watercress beds. Therefore, the risk concern for marine-estuarine fish is only

[24] Chronic toxicity data are not available for 1,2,4-triazole, TAA, or CGA-205375. TTR EECs only included CGA-205375 which is more likely similar to difenoconazole in terms of toxicity than the other two degradates (both are much less toxic than difenoconazole on an acute basis and ECOSAR suggests that they are less toxic on a chronic basis).

if and when difenoconazole-contaminated water is discharged into brackish receiving waterbodies.

Table 17. Chronic Risk Quotients for Freshwater and Estuarine/Marine Fish Exposed from the Proposed Difenoconazole Uses (TTR EEC)

Use	60-day EEC (μg/L)[1]	Freshwater and Estuarine/Marine Chronic RQ (NOAEC = 0.86 μg/L)
Guava/Papaya	2.7-4.3[2]	**3.1-5.0**
Cranberry (dry harvest)	5.4-7.6[2]	**6.3-8.8**
Cranberry (wet harvest & winter flood – bog water)	9.4-11.2[3]	**10.9-13.0**
Watercress	2.4[4]	**2.8**

[1] See **Appendix C, Table C-1**.
[2] Range representing ground and aerial applications.
[3] Range representing scenarios resulting in the lowest (Oregon) and highest (Wisconsin) TTR EECs for aerial applications.
[4] EEC may underestimate exposure in receiving waters.
BOLD exceeds chronic LOC (1.0).

8.2.2 Aquatic Invertebrates

There is not an acute risk concern for aquatic freshwater invertebrates from the proposed uses except for watercress (RQs < 0.01 except = 0.06 for watercress; **Table 18**) within the context of the limitations of the exposure modeling (*see* **Section 8.2.4** regarding uncertainty for flooded-field cranberry). The acute listed-species (estuarine/marine) RQ is exceeded for cranberry use (dry and wet harvest) and watercress.

Table 18. Acute Risk Quotients for Freshwater and Estuarine/Marine Invertebrates Exposed from the Proposed Difenoconazole Uses (TTR EEC)

Use	Peak EEC (μg/L)[1]	Freshwater Acute RQ (LC_{50} = 770 μg/L)	Estuarine/Marine Acute RQ (LC_{50} = 150 μg/L)
Guava/Papaya	3.2-5[2]	<0.01	<0.03
Cranberry (dry harvest)	5.7-8.3[2]	≤0.01	0.04-**0.06**
Cranberry (wet harvest & winter flood – bog water)	10.5-11.8[3]	≤0.02	**0.07-0.08**
Watercress	38.7	**0.05**	**0.26**

[1] See **Appendix C, Table C-1**.
[2] Range representing ground and aerial applications.
[3] Range representing scenarios resulting in the lowest (Oregon) and highest (Wisconsin) 1-day average TTR EECs for aerial applications.
BOLD exceeds acute listed-species LOC (0.05).

There is a chronic risk concern for aquatic invertebrates (listed and non-listed species) for the proposed uses. The chronic LOC (1.0) is exceeded for both freshwater and estuarine/marine water-column invertebrates (**Table 19**). There is not an LOC exceedance for freshwater invertebrates residing in watercress beds; however, there is considerable uncertainty regarding potential chronic exposure in receiving waterbodies downstream of watercress beds (*see* **Section**

8.2.4). Despite uncertainty about degradate chronic toxicity[25], the chronic LOC (1.0) is exceeded in most cases based on both TTR EECs and difenoconazole-only EECs (21-day difenoconazole-only EECs > NOAEC; *see* **Appendix C**, **Table C-1 and Table 19**). Although there are a couple exceptions, there is reasonable confidence in the assumption of equivalent toxicity of CGA-205375 and difenoconazole and so there is reasonable confidence in the risk assessment and conclusions based on TTR EECs. As discussed in detail elsewhere (USEPA, 2014), there are three available mysid life-cycle studies and there is uncertainty about the NOAEC for estuarine/marine invertebrates. In most cases there is an LOC exceedance based on even the least conservative (*i.e.*, least toxic) NOAEC from those studies (*see* **Table 19** and **footnotes 4** and **7**). Consequently, while there is not uncertainty about the potential risk concern for the proposed uses, there is uncertainty about the magnitude of the RQs.

Table 19. Chronic Risk Quotients for Freshwater and Estuarine/Marine Invertebrates Exposed from the Proposed Difenoconazole Uses (TTR EEC)

Use	21-day EEC (μg/L)[1]	Freshwater Chronic RQ (NOAEC = 5.6 μg/L)	Estuarine/Marine Chronic RQ (NOAEC = 4.8 μg/L)[2]
Guava/Papaya	2.8-4.5[3]	≤0.80	0.58-0.94[4]
Cranberry (dry harvest)	5.5-7.9[5]	0.98-**1.4**	**1.1-1.6**[4]
Cranberry (wet harvest & winter flood – bog water)	10.2-11.7[5]	**1.8-2.1**	**2.1-2.4**[4]
Watercress	3.9[6]	0.70	0.81[7]

[1] See **Appendix C, Table C-1**.
[2] This NOAEC is an upper bound estimate on toxicity. Two additional toxicity studies showed NOAECs < 0.31 and <0.115 μg/L.
[3] Range representing ground and aerial applications.
[4] Lower bound estimate of risk. **RQs > 1.0** for all use scenarios based on other available toxicity estimates (NOAEC < 0.115 and < 0.31 μg/L) as well as an acute-to-chronic toxicity estimate of the NOAEC (1.1 μg/L) (*see* USEPA, 2014 for details)
[5] Range representing scenarios resulting in the lowest (Oregon) and highest (Wisconsin) TTR EECs for aerial applications.
[6] EEC may underestimate exposure in receiving waters.
[7] Lower bound estimate of risk. **RQs > 1.0** based on other available toxicity estimates (NOAEC < 0.115 and < 0.31 μg/L) as well as an acute-to-chronic toxicity estimate of the NOAEC (1.1 μg/L) (*see* USEPA, 2014 for details)
BOLD exceeds chronic LOC (1.0).

Although there is an LOC exceedance for acute and chronic estuarine/marine invertebrates residing in cranberry bog water or watercress beds; it is assumed that freshwater is used for flooding these systems. Therefore, the potential risk concern for marine-estuarine invertebrates from flooded cranberry bogs or watercress beds is only if and when difenoconazole-contaminated water is discharged into brackish receiving waterbodies.

Risk to benthic invertebrates was considered given the fate properties of difenoconazole. Risk was not assessed using the submitted chronic toxicity range-finding study (MRID 47648601) due to problems with the study design. Instead, risk to benthic invertebrates was considered using water column invertebrate data (*Daphnia* and *Americamysis*) as surrogates. Pore water

---

[25] Data are not available for 1,2,4-triazole, TAA, or CGA-205375. TTR EECs only included CGA-205375 which is more likely similar to difenoconazole in terms of toxicity than the other two degradates (both are much less toxic than difenoconazole on an acute basis and ECOSAR suggests that they are less toxic on a chronic basis).

concentrations are relatively similar to (papaya, guava, and cranberry) or lower than (watercress) water column concentrations (**Appendix C, Table C-1 and Table C-2**); therefore, the risk concern for water column species is protective of benthic species in general (*i.e.*, there is a risk concern); however, risk may be over or underestimated and the magnitude of the RQ associated with that concern is uncertain without toxicity data for benthic invertebrates.

8.2.3 Aquatic Plants

There is not a risk concern for aquatic plants from the proposed uses within the context of the limitations of the exposure modeling (*see* **Section 8.2.4** regarding uncertainty for flooded-field cranberry and watercress). The LOC (1.0) is not exceeded for non-listed or listed species (RQs ≤ 0.73; **Table 20**). Although there is uncertainty about degradate toxicity[26], it is unlikely that the risk conclusions are impacted.

Table 20. Risk Quotients for Aquatic Plants Exposed to Difenoconazole from the Proposed Difenoconazole Uses (TTR EEC)

Use	Peak EEC (µg/L)[1]	Vascular Plant Non-listed RQ (EC_{50} = 1900 µg/L)	Vascular Plant Listed RQ (EC_{05} = 110 µg/L)	Non-vascular Plant Non-listed RQ (EC_{50} = 98 µg/L)	Non-vascular Plant Listed RQ (NOAEC = 53 µg/L)
Guava/Papaya	3.2-5[2]	<0.01	≤0.05	≤0.05	≤0.09
Cranberry (dry harvest)	5.7-8.3[2]	<0.01	≤0.08	≤0.09	≤0.16
Cranberry (wet harvest & winter flood – bog water)	10.5-11.8[3]	<0.01	≤0.11	≤0.12	≤0.22
Watercress	38.7	0.02	0.35	0.40	0.73

[1] See **Appendix C, Table C-1**.
[2] Range representing ground and aerial applications.
[3] Range representing scenarios resulting in the lowest (Oregon) and highest (Wisconsin) 1-day average TTR EECs for aerial applications.
BOLD exceeds listed-species or non-listed species LOC (1.0).

8.2.4 Uncertainties about EECs for Cranberry (flooded-field only) and Watercress

Exposure and risk from flooded-field cranberry and watercress uses is highly dependent on the processing of water used for production. As previously discussed, the modeled EECs are intended to represent exposure in the cranberry bog or watercress bed. They are also used to assess risk in downstream receiving water bodies (*i.e.*, waterbodies that receive the difenoconazole-contaminated water released from the bog or bed). The EECs for the cranberry bog, watercress bed, and release water are based on a point to point flow of uncontaminated water through a single difenoconazole-treated bog or watercress bed. The EECs do not account for recycling of that same water back through the same difenoconazole-treated bog or watercress bed. Likewise, the EECs do not account for recycling of water through multiple difenoconazole-

[26] Data are not available for TAA or CGA-205375. TTR EECs only included CGA-205375 which is more likely similar to difenoconazole in terms of toxicity than TAA (based on ECOSAR estimates).

treated bogs or beds. In both cases, the practice of recycling may lead to greater exposure concentrations given that difenoconazole is a relatively persistent compound.

The modeled chronic EECs for the watercress bed may underestimate exposure in receiving water bodies (independent of the additional uncertainty about recycling of water discussed above). This is because the watercress bed is a continuous flow through system of 0.5 to 1.5-inch depth of water. Therefore, 21-day and 60-day EECs may not be representative of receiving waters with longer holding periods. Any LOC exceedance based on the modeled EECs is supportive of a potential risk concern in the bed and receiving water bodies whereas the lack of an exceedance based on those EECs does not rule out a potential concern in receiving water bodies.

EECs in receiving water bodies may be lower than those estimated in the cranberry bog and watercress bed through processes such as degradation in the water column, absorption by sediment, and dilution with uncontaminated water from other sources in the adjacent waterways. Additionally, exposure in certain receiving water bodies could be further reduced due to label restrictions on releasing effluent containing difenoconazole into lakes, streams, ponds, estuaries, oceans, or other waters in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES).

8.3 Risk Summary

Consistent with previously assessed uses, the primary risk concerns from the proposed uses are for chronically exposed listed and non-listed aquatic invertebrate, fish, bird, and mammal species. In addition, there is an acute risk concern for listed aquatic invertebrate species and a risk concern cannot be precluded for terrestrial dicots (listed species) or honeybees based on the available data.

There is uncertainty regarding risk to aquatic organisms and birds and mammals that prey on fish and aquatic invertebrates for flooded-field cranberry and watercress uses. Water use practices at individual production facilities are expected to vary and can impact exposure estimates in different waterbodies associated with the production (*i.e.*, cranberry bog, watercress bed, and receiving water bodies). In cases where the LOC was exceeded (e.g., chronic risk to fish) there is greater certainty about the overall risk concern than the RQ itself. In cases where the LOC was not exceeded (e.g., acute risk to fish), practices such as recycling at an individual facility could potentially lead to a risk concern if exposure concentrations are high enough.

References

Hutchinson, L. 2005. Ecological Aquaculture: A sustainable Solution. Permanent Publications, Hyden House Ltd, East Meon, Hampshire, England

Petit, A.-N., F. Fontaine, P. Vatsa, C. Clement, and N. Vaillant-Gaveau. 2012. Fungicide Impacts on Photosynthesis in Crop Plants. Photosynth. Res. 111:315-326.

USDA, 2015. Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen.

USEPA, 2006. Triazole Alanine, Triazole Acetic Acid: Drinking Water Assessment in Support of Reregistration and Registration Actions for Triazole-derivative Fungicide Compounds. Risk Assessment Type: Single Chemical Aggregate. Environmental Fate and Effects Division, Office of Chemical Safety and Pollution Prevention. D320682

USEPA, 2007. Section 3 New Use: Environmental Fate and Ecological Risk Assessment for Difenoconazole. Environmental Fate and Effects Division, Office of Chemical Safety and Pollution Prevention. D333319 and D340041

USEPA, 2009a. Guidance for Selecting Input Parameters in Modeling the Environmental Fate and Transport of Pesticides (Version 2.1; Oct. 22, 2009). Environmental Fate and Effects Division, Office of Chemical Safety and Pollution Prevention.

USEPA, 2009b. Ecological Risk Assessment for the Section 3 New Use Registration of Difenoconazole on Bulb Vegetables, Brassica (Cole) Leafy Vegetables, Cucurbit Vegetables, Citrus Fruit, Grapes, and Tree Nuts. Environmental Fate and Effects Division, Office of Chemical Safety and Pollution Prevention. D361251.

USEPA, 2010. Ecological Risk Assessment for the Section 3 New Use Registration of Difenoconazole on Golf Course Turf. Environmental Fate and Effects Division, Office of Chemical Safety and Pollution Prevention. D377719.

USEPA, 2013a. Guidance on modeling off-site deposition of pesticides via spray drift for ecological and drinking water assessments. Environmental Fate and Effects Division, Office of Chemical Safety and Pollution Prevention.

USEPA, 2013b. Ecological Risk Assessment for the Proposed New Use of Difenoconazole on Canola and Oilseed Subgroup 20A. Environmental Fate and Effects Division, Office of Chemical Safety and Pollution Prevention. DP 409484 and 409488

USEPA, 2014. Difenoconazole: Ecological Risk Assessment for Numerous Proposed New Uses and Changes to Registered Uses (Application Rate, Crop Groupings, and Additions to New Products. Environmental Fate and Effects Division, Office of Chemical Safety and Pollution Prevention. DP 417610+

USEPA, 2015. Difenoconazole: Preliminary Problem Formulation for Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Exposure Assessments in Support of Registration Review. Environmental Fate and Effects Division, Office of Chemical Safety and Pollution Prevention. DP 428500

USEPA, 2016. Difenoconazole: Ecological Risk Assessment for Proposed New Uses on Cotton (including Cottonseed Crop Subgroup 20C), Rice, and Wild Rice. DP 432214

Appendix A: Representative KABAM Input and EECs (Guava/Papaya Use: Aerial)

Table A-1. Chemical characteristics of Difenoconazole

Characteristic	Value
Pesticide Name	Difenoconazole
Log K_{OW}	4.4
K_{OW}	25119
K_{OC} (L/kg OC)	5381
Time to steady state (T_S; days)	9
Pore water EEC (µg/L)	3.9 (4 day surface water TTR EEC)
Water Column EEC (µg/L)	4.8 (4 day surface water TTR EEC)

Table A-2. Mammalian and avian toxicity data for Difenoconazole

Animal	Measure of effect (units)	Value	Species
Avian	LD_{50} (mg/kg-bw)	2150	mallard duck
	LC_{50} (mg/kg-diet)	4579	Northern bobwhite quail
	NOAEC (mg/kg-diet)	21.9	Northern bobwhite quail
	Mineau Scaling Factor	1.15	Default value for all species is 1.15 (for chemical specific values, see Mineau et al. 1996).
Mammalian	LD_{50} (mg/kg-bw)	1453	laboratory rat
	LC_{50} (mg/kg-diet)	N/A	other
	Chronic Endpoint	25	laboratory rat
	units of chronic endpoint*	ppm	

Table A-3. Calculation of EECs for mammals and birds consuming fish contaminated by Difenoconazole

Wildlife Species	Biological Parameters				EECs (pesticide intake)	
	Body Weight (kg)	Dry Food Ingestion Rate (kg-dry food/kg-bw/day)	Wet Food Ingestion Rate (kg-wet food/kg-bw/day)	Drinking Water Intake (L/d)	Dose Based (mg/kg-bw/d)	Dietary Based (ppm)
Mammalian						
fog/water shrew	0.02	0.140	0.585	0.003	2.657	4.54
rice rat/star-nosed mole	0.1	0.107	0.484	0.011	2.190	4.53
small mink	0.5	0.079	0.293	0.048	1.860	6.34
large mink	1.8	0.062	0.229	0.168	1.453	6.34
small river otter	5.0	0.052	0.191	0.421	1.212	6.34
large river otter	15.0	0.042	0.157	1.133	1.090	6.94
Avian						
sandpipers	0.0	0.228	1.034	0.004	4.6952	4.54
cranes	6.7	0.030	0.136	0.211	0.6305	4.64
rails	0.1	0.147	0.577	0.010	3.0582	5.30
herons	2.9	0.040	0.157	0.120	0.8563	5.44
small osprey	1.3	0.054	0.199	0.069	1.2644	6.34
white pelican	7.5	0.029	0.107	0.228	0.7403	6.94

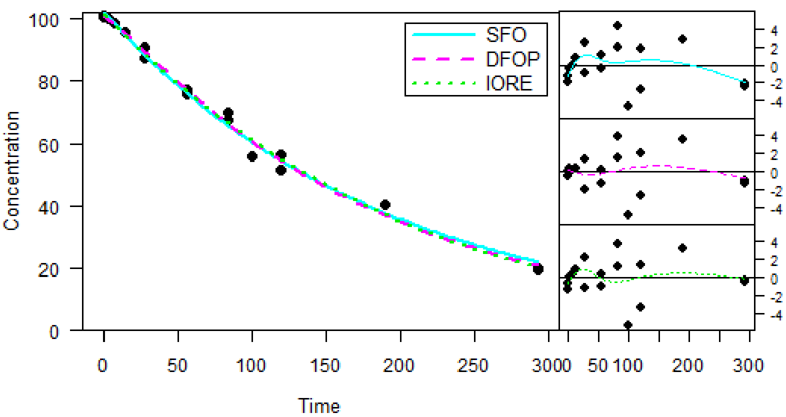
Appendix B: Calculation of DT_{50} for TTR (difenoconazole + CGA-205375)

The DT_{50}s for TTR (difenoconazole + CGA-205375) were calculated for selected environmental fate properties using the PestDF (Ver. 0.8.4; March 23, 2015) tool[27], a NAFTA Guidance for Evaluating and Calculating Degradation Kinetics in Environmental media. Calculations of DT_{50}s were made for various environmental media. The model recommended DT_{50}s are in red color.

Soils

MRID 46950109- Aerobic soil Metabolism

DATS	%
0	101.
0	100.
3	100.
7	98.6
7	98.6
14	95.8
28	87.4
28	90.8
56	77.3
56	75.9
84	67.8
84	70.2
100	55.8
120	51.7
120	56.3
190	40.5
293	19.6
293	19.8

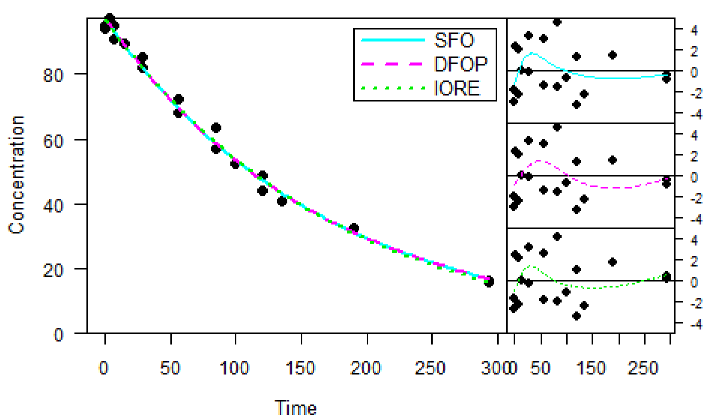


	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	132	439	2.4	102	k = 0.00525
DFOP	133	425	2.5	101	f = -0.0454, k_0 = 0.0542, k_1 = 0.00553
IORE	135	396	2.4	102	N = 0.844, k = 0.01

S_C	90.4
S_{SFO}	88.8
Slow $t_{1/2}$	125
$t_{R\ IORE}$	119

MRID: 46950110: Aerobic Soil Metabolism

DAT	(% of applied)
0	95.0
0	93.9
3	97.5
7	95.0
7	90.6
14	89.2
28	85.3
28	81.9
56	67.9
56	72.4
84	63.3
84	57.1
100	52.6
120	44.1
120	48.6
135	41.0
190	32.6
293	16.4
293	16.0



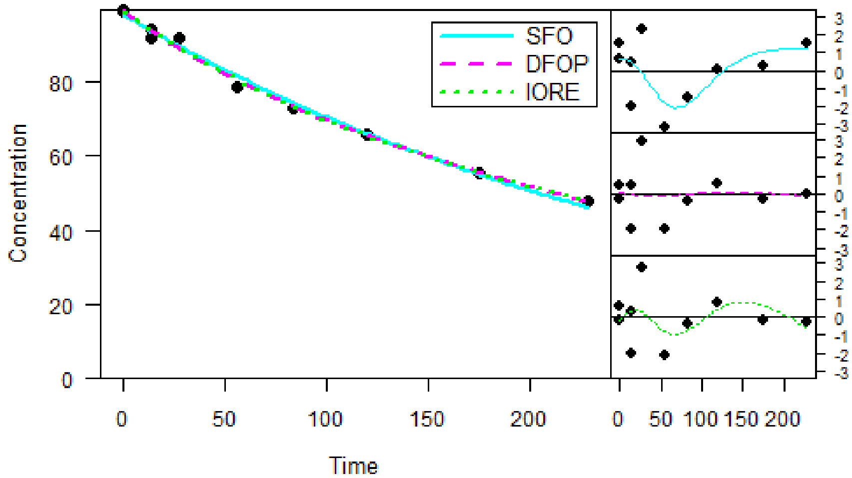
	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	116	386	1.8	97	k = 0.00597
DFOP	116	386	2	97	f = 0.379, k_0 = 0.00597, k_1 = 0.00597
IORE	117	367	1.9	96.7	N = 0.922, k = 0.00822

S_C	106
S_{SFO}	94.6
Slow $t_{1/2}$	116
$t_{R\ IORE}$	110

[27] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/guidance-calculate-representative-half-life-values

MRID: 46950111_Schanz sandy loam Soil

DAT	(% applied)
0	98.9
0	99.7
14	94.2
14	91.8
28	91.8
56	78.5
84	72.9
120	66.1
120	66.1
175	55.3
228	47.7

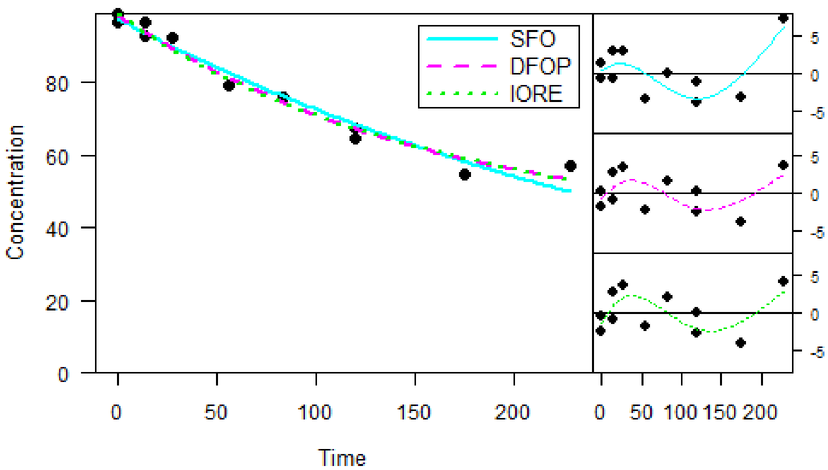


	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	209	696	1.7	98.2	$k = 0.00331$
DFOP	215	787	1.5	99.2	$f = 0.091$, $k_0 = 0.0179$, $k_1 = 0.0028$
IORE	216	1179	1.4	99.1	$N = 1.54$, $k = 0.00032$

S_C	23.9
S_{SFO}	26.1
Slow $t_{1/2}$	247
$t_{R\ IORE}$	355

MRID: 46950111_Pappelacker sandy loam/loamy sand

DAT	(% applied)
0	96.7
0	98.8
14	96.4
14	92.8
28	92.6
56	79.1
84	76.1
120	64.6
120	67.3
175	54.9
228	57.0

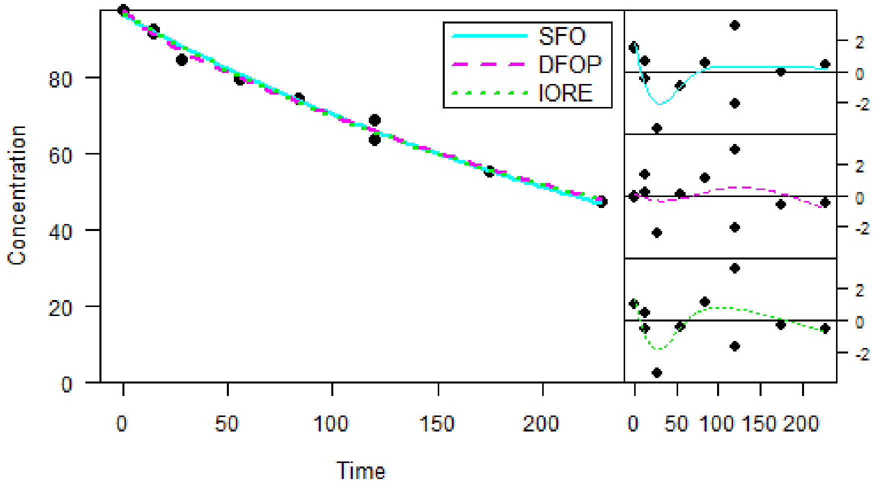


	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	235	780	3.4	97.6	$k = 0.00295$
DFOP	NA	NA	2.9	98.7	$f = 0.865$, $k_0 = 0.00456$, $k_1 = -0.00243$
IORE	264	3241	2.9	99.2	$N = 2.26$, $k = 1.3e-05$

S_C	98.4
S_{SFO}	111
Slow $t_{1/2}$	-286
$t_{R\ IORE}$	976

MRID: 46950111_Senozan silty clay loam

DAT	% applied
0	97.9
0	98.0
14	91.8
14	92.9
28	84.7
56	79.9
84	74.6
120	69.0
120	64.0
175	55.5
228	47.4

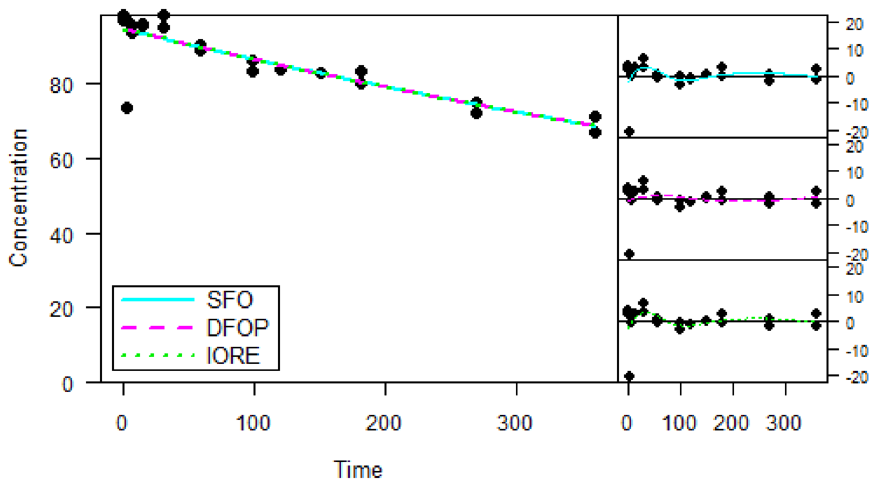


	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	220	730	1.5	96.5	$k = 0.00315$
DFOP	220	762	1.2	98.1	$f = 0.0389$, $k_0 = 0.0829$, $k_1 = 0.00297$
IORE	225	981	1.5	96.9	$N = 1.32$, $k = 0.000816$

S_C	40
S_{SFO}	32.3
Slow $t_{1/2}$	234
$t_{R\ IORE}$	295

MRID: 46950112 & 13-Soil

DAT	% applied
0	96.8
0	98.3
3	73.6
3	96.9
7	93.4
7	95.6
15	96.0
15	95.6
30	98.5
30	95.0
58	90.4
58	89.1
99	86.0
99	83.1
120	83.7
120	83.6
150	82.9
150	82.8
181	79.9
181	83.1
269	74.8
269	72.2
360	66.8
360	71.1

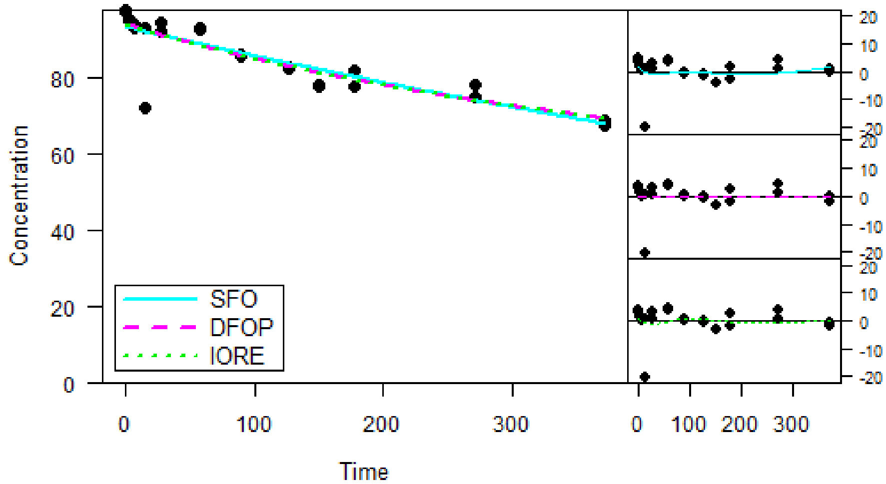


	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	777	2580	3.1	94.5	$k = 0.000893$
DFOP	780	2606	3.3	94.5	$f = 0.00913$, $k_0 = 0.00263$, $k_1 = 0.00088$
IORE	788	2769	3.2	94.5	$N = 1.07$, $k = 0.000659$

S_C	623
S_{SFO}	558
Slow $t_{1/2}$	788
$t_{R\ IORE}$	834

MRID: 46950114 & 15_Soil

DAT	% applied
0	97.0
0	97.7
3	94.6
3	95.1
7	93.9
7	92.8
15	71.9
15	92.8
27	94.2
27	91.9
58	92.2
58	92.7
90	85.4
90	86.1
127	82.5
127	82.2
150	77.7
150	77.8
178	77.5
178	81.7
272	78.0
272	74.8
372	67.4
372	68.9



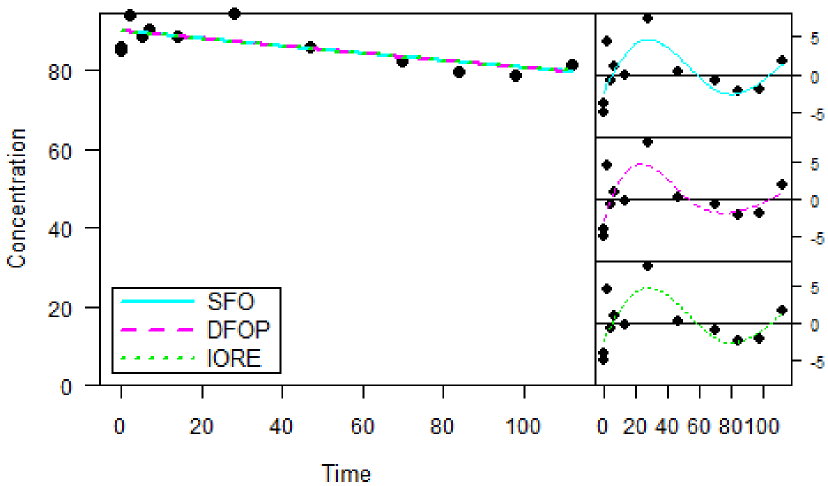
	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	813	2700	3.5	93.1	k = 0.000853
DFOP	1639	10159	3.7	93.7	f = 0.323, k_0 = 0.00295, k_1 = 0.000188
IORE	1361	49578	3.5	93.8	N = 3.07, k = 9.38e-08

S_C	608
S_{SFO}	556
Slow $t_{1/2}$	3.68e+03
$t_{R\ IORE}$	1.49e+04

<u>Aerobic Aquatic Metabolism</u>

MRID: 46950117+ Aerobic metabolism of difenoconazole ir

DAT	(% of Applied)
0	85.0
0	86.1
2	94.3
5	88.8
7	90.3
14	88.5
28	94.8
47	85.9
70	82.6
84	79.9
98	79.
112	81.5

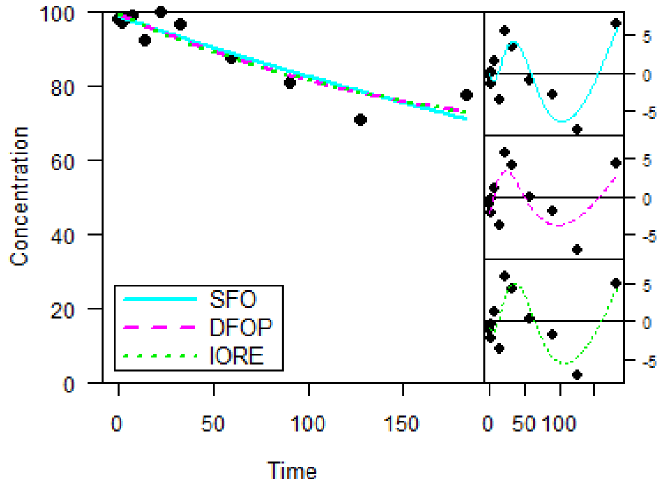


	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	639	2123	2.9	90	k = 0.00108
DFOP	615	1957	3.2	90.1	f = -0.169, k_0 = 0.00219, k_1 = 0.00124
IORE	819	5760	3.1	90	N = 1.78, k = 3.31e-05

S_C	168
S_{SFO}	130
Slow $t_{1/2}$	557
$t_{R\ IORE}$	1.73e+03

MRID: 46950116-Aerobic metabolism of difenoconazole in

Days Posttreatment	(% of Applied)
0	98.1
1	96.7
3	98.1
7	98.7
14	92.3
22	100.
32	96.4
59	87.5
90	80.8
127	71.0
183	77.4

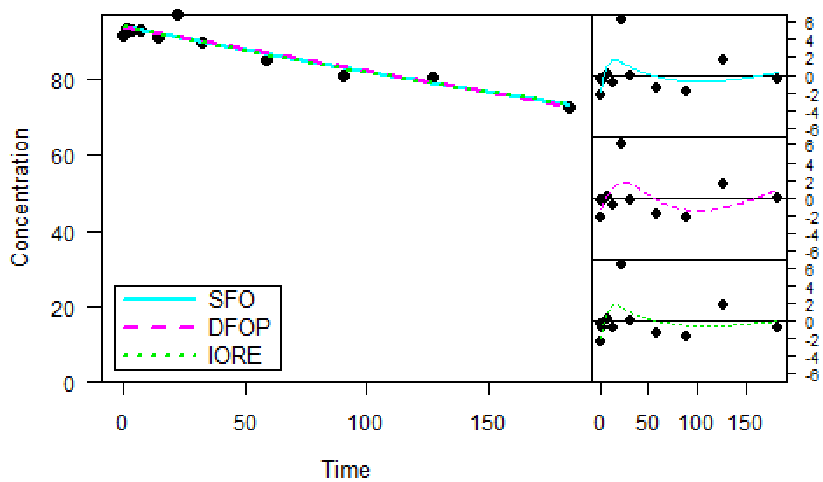


	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	387	1286	3.5	98.4	k = 0.00179
DFOP	NA	NA	3.5	99.2	f = 0.888, k_0 = 0.00303, k_1 = -0.00386
IORE	689	37810	3.4	99.2	N = 3.36, k = 5.01e-08

S_C	
S_{SFO}	
Slow $t_{1/2}$	
$t_{R\ IORE}$	

MRID: 46950116:AAQM_difenoconazole in two Swiss wate

DAT	(% of Applied)
0	91.5
1	93.3
3	92.8
7	93.1
14	91.2
22	97.3
32	89.7
59	85.1
90	81.1
127	80.6
183	72.7



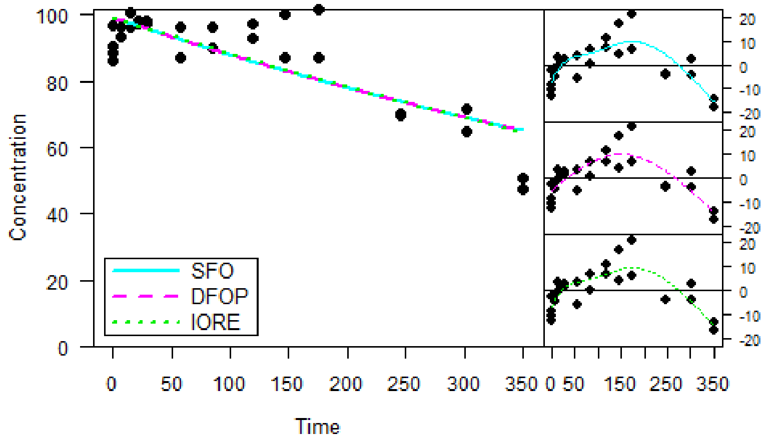
	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	510	1693	2	93.8	k = 0.00136
DFOP	450	1307	2.2	93.6	f = -0.314, k_0 = 0.00439, k_1 = 0.00196
IORE	596	3486	2.1	93.9	N = 1.61, k = 8.99e-05

S_C	73.1
S_{SFO}	54.5
Slow $t_{1/2}$	353
$t_{R\ IORE}$	1.05e+03

Anaerobic Aquatic Metabolism

MRID 46950119+Anaerobic metabolism in California river w

DAT	(% of Applied)
0	96.5
0	86.0
0.04	88.4
0.04	90.4
7	96.3
7	93.3
15	96.3
15	101.
22	96.9
22	98.0
29	98.2
29	97.1
57	96.
57	86.9
85	90.0
85	96.2
119	92.7
119	97.1
147	100.
147	87.3
175	86.8
175	102.
245	70.1
245	69.7
302	64.7
302	71.6
350	50.8



	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	577	1918	7.3	99	k = 0.0012
DFOP	577	1918	7.8	99	f = 0.315, k_0 = 0.0012, k_1 = 0.0012
IORE	537	1316	7.3	99.1	N = 0.577, k = 0.00781

S_C	2.15e+03
S_{SFO}	2.06e+03
Slow $t_{1/2}$	577
$t_{R\ IORE}$	396

Appendix C: Aquatic EECs

Table C-1. Surface Water EECs

Water Source (model)	Use (rate and interval)	Crop Scenario	Application Method	Peak EEC (µg/L)	21-Day EEC (µg/L)	60-Day EEC (µg/L)
	Concentrations (EECs) of Difenoconazole only					
Surface Water (PWC)	Guava and Papaya (4 application @ 0.115 lb a.i./A)	FLAvocadoSTD	Aerial	3.2	2.7	2.5
			Ground	2.2	1.7	1.6
	Cranberry (dry harvest) (3 application @ 0.115 lb a.i./A)	ORBerriesOP	Aerial	5.1	4.6	4.4
			Ground	3.3	3.1	3.0
Surface water (PFAM)[a]	Cranberry (wet harvest & winter flood – bog water) (3 application @ 0.115 lb a.i./A)	Massachusetts	Aerial	7.3[b]	7.1	6.2
		Oregon		7.0[b]	6.9	6.3
		Wisconsin		7.5[b]	7.5	7.1
	Watercress (4 application @ 0.115 lb a.i./A)	Florida		36.7	3.7	2.4
	Concentrations (EECs) of Total Toxic Residues (Difenoconazole and MI [CGA 205375])					
Surface Water (PWC)	Guava and Papaya (4 application @ 0.115 lb a.i./A)	FLAvocadoSTD	Aerial	5.0	4.5	4.3
			Ground	3.2	2.8	2.7
	Cranberry (dry harvest) (3 application @ 0.115 lb a.i./A)	ORberriesOP	Aerial	8.3	7.9	7.6
			Ground	5.7	5.5	5.4
Surface water (PFAM)[a]	Cranberry (wet harvest & winter flood – bog water) (3 application @ 0.115 lb a.i./A)	Massachusetts	Aerial	11.6[b]	11.0	9.6
		Oregon		10.5	10.2	9.4
		Wisconsin		11.8	11.7	11.2
	Watercress (4 application @ 0.115 lb a.i./A)	Florida		38.7	3.9	2.4

[a] EECs generated using PFAM represent concentration in bog water of cranberry field or water in watercress bed.
[b] 1-day average concentration

Table C-2. Pore Water EECs

Water Source (model)	Use (rate and interval)	Crop Scenario	Application Method	Peak EEC (µg/L)	21-Day EEC (µg/L)	60-Day EEC (µg/L)
	Concentrations (EECs) of Difenoconazole only					
Surface Water (PWC)	Guava and Papaya (4 application @ 0.115 lb a.i./A)	FLAvocadoSTD	Aerial	2.2	2.2	NA
			Ground	1.4	1.4	NA
	Cranberry (dry harvest) (3 application @ 0.115 lb a.i./A)	ORBerriesOP	Aerial	4.2	4.2	NA
			Ground	2.9	2.9	NA
Surface water (PFAM)[a]	Cranberry (wet harvest & winter flood – bog water) (3 application @ 0.115 lb a.i./A)	Massachusetts	Aerial	14.7[b]	14.4	NA
		Oregon		14.5[b]	14.2	NA
		Wisconsin		15.5[b]	14.6	NA
	Watercress (4 application @ 0.115 lb a.i./A)	Florida		1.9	1.7	NA
	Concentrations (EECs) of Total Toxic Residues (Difenoconazole and MI [CGA 205375])					
Surface Water (PWC)	Guava and Papaya (4 application @ 0.115 lb a.i./A)	FLAvocadoSTD	Aerial	3.9	3.9	NA
			Ground	2.5	2.5	NA
	Cranberry (dry harvest) (3 application @ 0.115 lb a.i./A)	ORberriesOP	Aerial	7.4	7.4	NA
			Ground	5.2	5.2	NA
Surface water (PFAM)[a]	Cranberry (wet harvest & winter flood – bog water) (3 application @ 0.115 lb a.i./A)	Massachusetts	Aerial	21.1[b]	20.7	NA
		Oregon		20.5[b]	20.3	NA
		Wisconsin		22.5[b]	21.3	NA
	Watercress (4 application @ 0.115 lb a.i./A)	Florida		2.0	1.7	NA

[a] EECs generated using PFAM represent concentration in bog water of cranberry field or water in watercress bed.
[b] 1-day average concentration

Appendix D: Example Output of Pesticide in Water Calculator (PWC) Model

Estimated Environmental Concentrations for difenoconazole are presented in **Table D-1** for the USEPA standard pond with the ORberriesOP field scenario. A graphical presentation of the year-to-year peaks is presented in **Figure D-1**. These values were generated with the Pesticide Water Calculator (PWC), Version 1.52. Critical input values for the model are summarized in **Table D-2 and D-3**.

In the benthic region, pesticide dissipation is negligible (4218.1 days). The main source of dissipation in the benthic region is metabolism (effective average half-life = 4218.1 days). The vast majority of the pesticide in the benthic region (99.83%) is sorbed to sediment rather than in the pore water.

Table D-1. Estimated Environmental Concentrations (ppb) for Difenoconazole.

Peak (1-in-10 yr)	8.29
4-day Avg (1-in-10 yr)	8.12
21-day Avg (1-in-10 yr)	7.87
60-day Avg (1-in-10 yr)	7.64
365-day Avg (1-in-10 yr)	7.28
Entire Simulation Mean	5.12

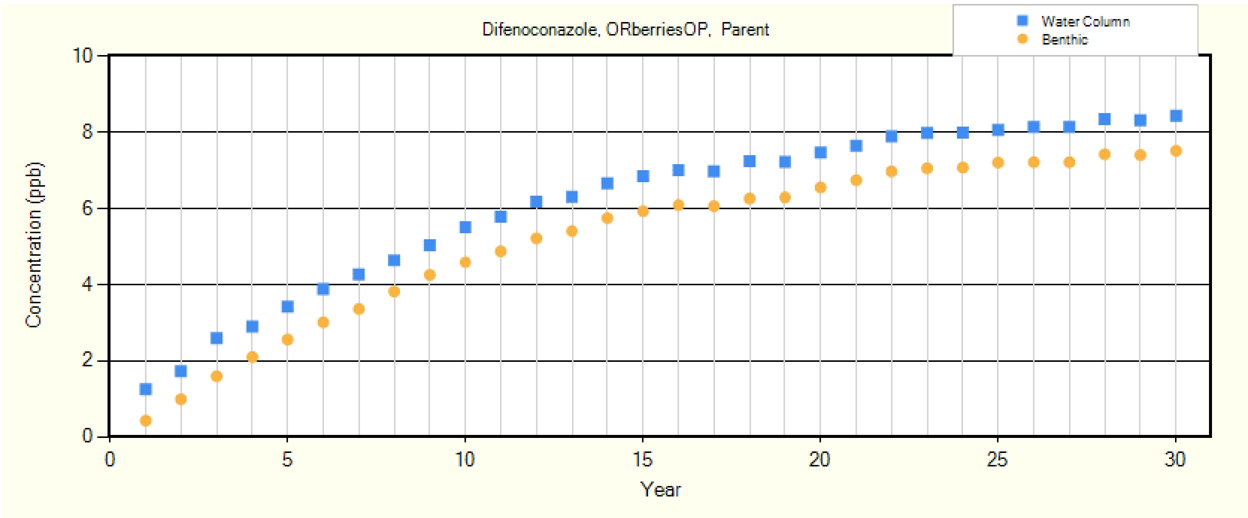
Table D-2. Summary of Model Inputs for Difenoconazole.

Scenario	ORberriesOP
Cropped Area Fraction	1
Koc (ml/g)	3981
Water Half-Life (days) @ 25 °C	649
Benthic Half-Life (days) @ 25 °C	1731
Photolysis Half-Life (days) @ 40 °Lat	0
Hydrolysis Half-Life (days)	0
Soil Half-Life (days) @ 25 °C	670
Foliar Half-Life (days)	
Molecular Weight	406.27
Vapor Pressure (torr)	2.5E-10
Solubility (mg/l)	15
Henry's Constant	0.0

Table D-3. Application Schedule for Difenoconazole.

Date (Days Since Emergence)	Type	Amount (kg/ha)	Eff.	Drift
30	Above Crop (Foliar)	0.129	0.95	0.125
37	Above Crop (Foliar)	0.129	0.95	0.125
51	Above Crop (Foliar)	0.129	0.95	0.125

Figure D-1. Yearly Peak Concentrations

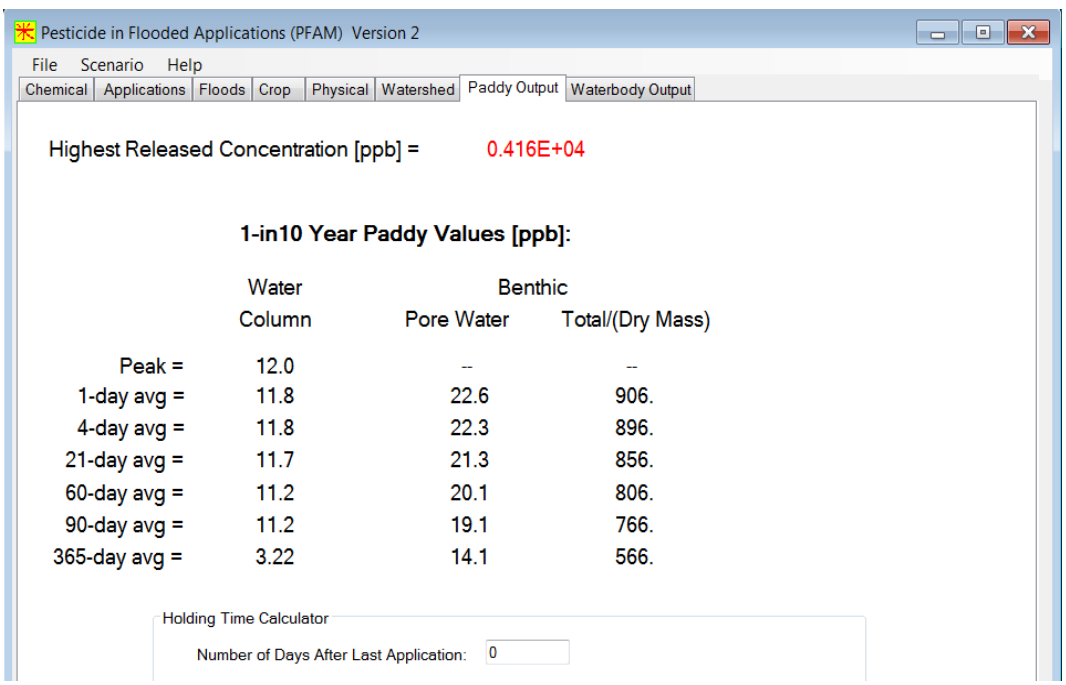


Appendix E: PFAM Flood Schedule Assumptions and Example Output

Cranberry

Cranberry Flood Schedule

WI Cranberry TTR


Pesticide in Flooded Applications (PFAM) Version 2

File Scenario Help

Chemical Applications Floods Crop Physical Watershed Paddy Output Waterbody Output

Highest Released Concentration [ppb] = 0.416E+04

1-in10 Year Paddy Values [ppb]:

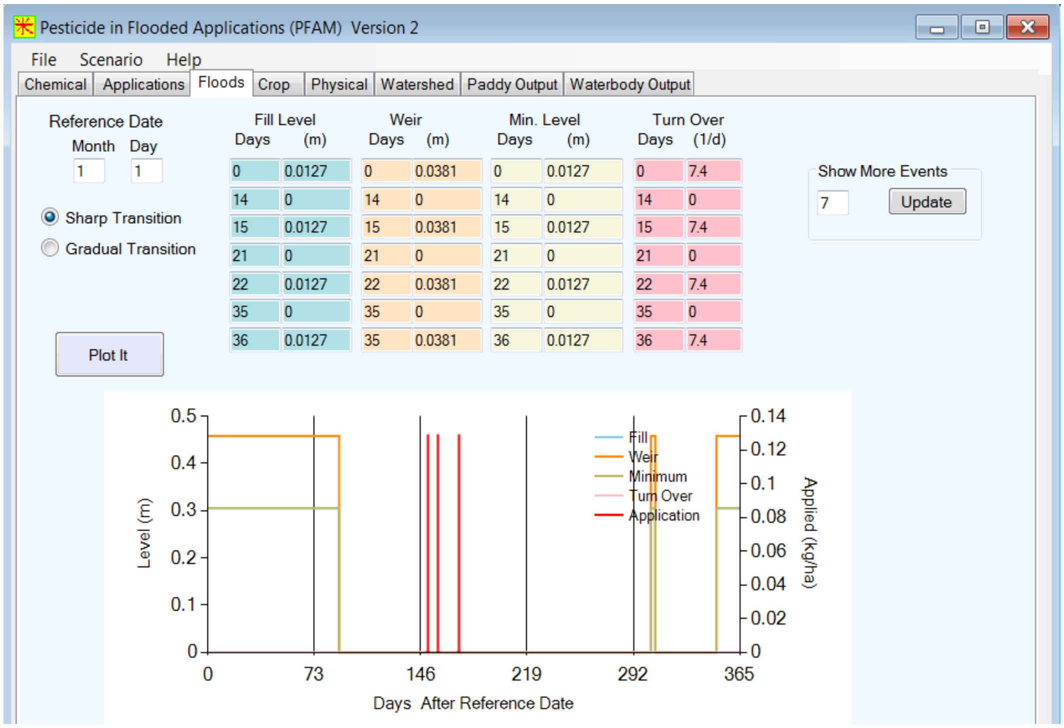
	Water Column	Benthic Pore Water	Benthic Total/(Dry Mass)
Peak =	12.0	--	--
1-day avg =	11.8	22.6	906.
4-day avg =	11.8	22.3	896.
21-day avg =	11.7	21.3	856.
60-day avg =	11.2	20.1	806.
90-day avg =	11.2	19.1	766.
365-day avg =	3.22	14.1	566.

Holding Time Calculator

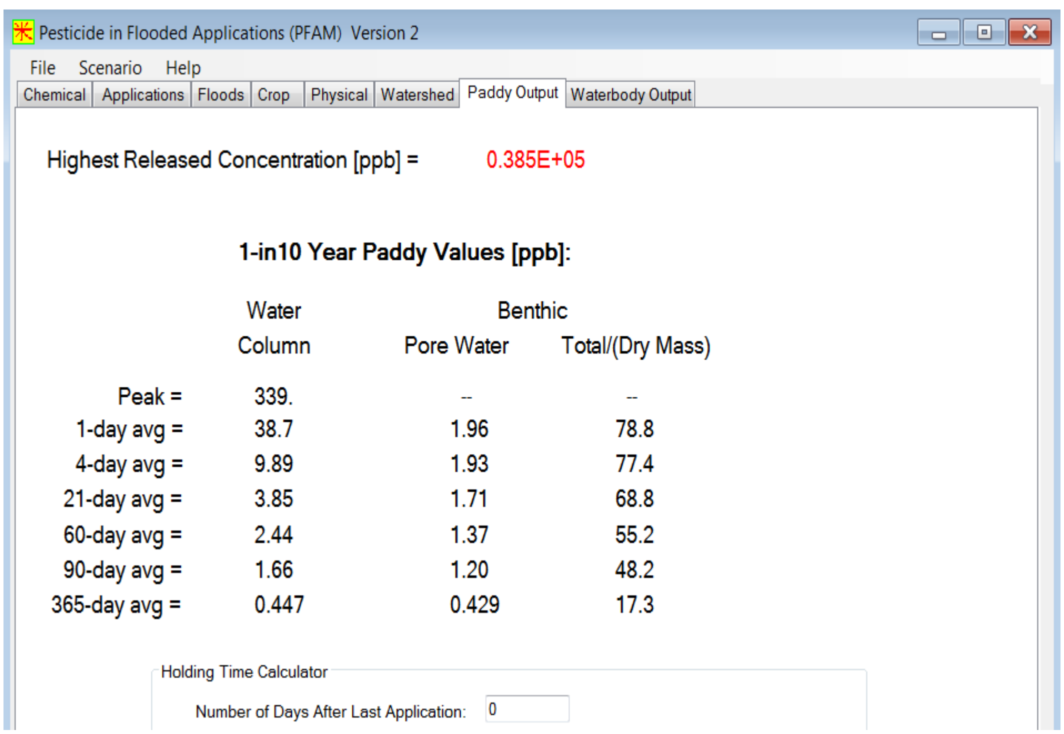
Number of Days After Last Application: 0

Watercress

Watercress Flood Schedule



FL Watercress TTR



Appendix F: ECOSAR Results

Table F-1. Comparative Aquatic Toxicity of Difenoconazole and Major Degradation Products

Compound	FW fish 96-hr acute LC_{50} (mg/L)	FW fish chronic NOAEC (mg/L)[1]	FW invertebrate 48-hr acute EC_{50} (mg/L)	FW invertebrate chronic NOAEC (mg/L)[1]	ME fish 96-hr acute LC_{50} (mg/L)	ME fish chronic NOAEC (mg/L)[1]	ME invertebrate 96-hr acute LC_{50} (mg/L)	ME invertebrate chronic NOAEC (mg/L)[1]	Non-vascular plant 96-hr EC_{50} (mg/L)
Difenoconazole	**0.87** (0.81)	**0.007** (0.0009)	**0.95** (0.77)	**0.030** (0.006)	(0.82)	(0.0009)	(0.15)	(<0.000115)	**0.51** (0.30)[2]
1,2,4-triazole	**722.0** (498.0)	**2.2**	**3166.2** (>98.0)	**29.2**	-	-	-		**35.7** (14.0)[2]
Triazole acetic acid	**51322.1** (>101.0)	**132.3**	**281000.0** (>108.0)	**2132.3**	-	-	-		**1716.9**
CGA-205375	**2.79**	**0.022**	**2.6**	**0.179**	**8.36**[3]	**0.099**	**0.870**	**0.252**	**1.33**

[1] ECOSAR estimated chronic value is defined as the geometric mean of the no observed effect concentration (NOEC) and the lowest observed effect concentration (LOEC).

[2] Green algae

[3] Endpoint exceeds water solubility of compound (1,2,4-triazole = 700,000 mg/L; TAA = 1,000,000 mg/L; CGA-205375 = 3.57 mg/L). (TAA and CGA-205375 are EPISuite estimates)

BOLD values are ECOSAR (v1.00) toxicity estimates (lowest toxicity value of multiple ECOSAR classes is shown, *i.e.*, the most toxic).

Italic values are from submitted toxicity studies (most sensitive endpoint if multiple are available)

FW = freshwater and ME = marine/estuarine